Volume 14, Number 6
DECEMBER 1953

Postgraduate Medicine

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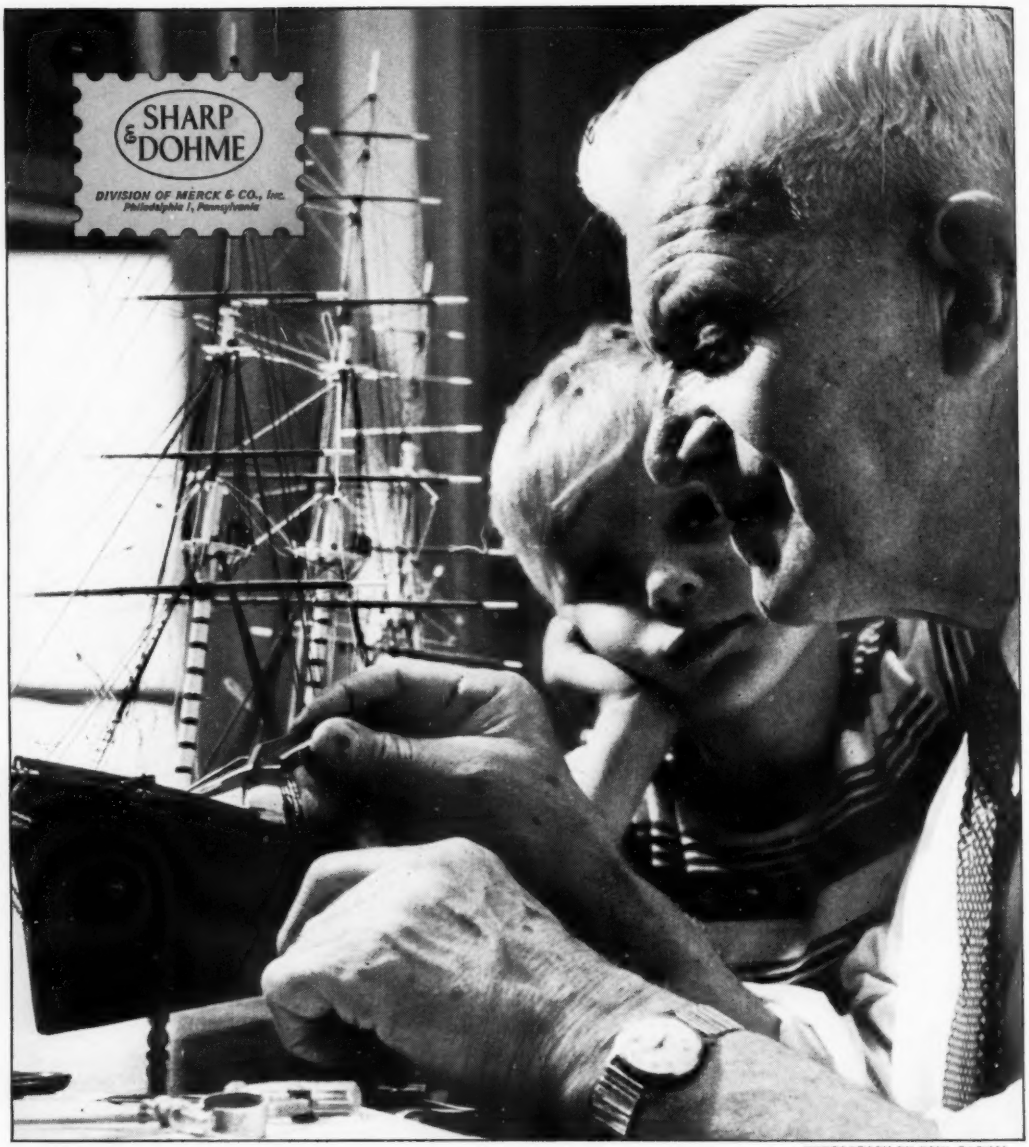

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Postgraduate Medicine

Volume 14 · Number 6
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OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

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Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by members of POSTGRADUATE MEDICINE'S *Editorial Advisory Board and other consultants.*

• ETHYLENE DISULPHONATE

Question: Would you please discuss the use of ethylene disulphonate in extrinsic asthma and other allergies? I have heard it is widely used in Belgium and England but I do not recall any articles in the well-known American journals on the use of this drug.

M.D.—New York

ANSWER: Ethylene disulphonate was first reported by Evans. G., Bodman, J. and Maisin, J. H. (Med. Press & Circ. 203:5273, 1940) as a means of treating an allergic state. Reports of protective action could not be confirmed by Fisk, R. T., Small, W. S. and Foord, A. G. (J. Allergy 15:14, 1944). Some favorable clinical reports were given by Smith, N. M. (Clin. Med. 51:323, 1944), Wasson, V. P. (Arch. Pediat. 60:511, 1943) and Bartlett, C. L. (Arch. Pediat. 61:311, 1944). These could not be confirmed by Archibald, H. C. (Arch. Pediat. 62:219, 1945), Kurland, L. T. and Bubert, J. M. (Bull. School Med. Univ. Maryland 30:46, 1945).

These investigators reported the preparation to have "little if any therapeutic value" and advised caution against its continued use.

This material was used quite extensively through the West and Midwest but I do not believe it is being used at the present time.

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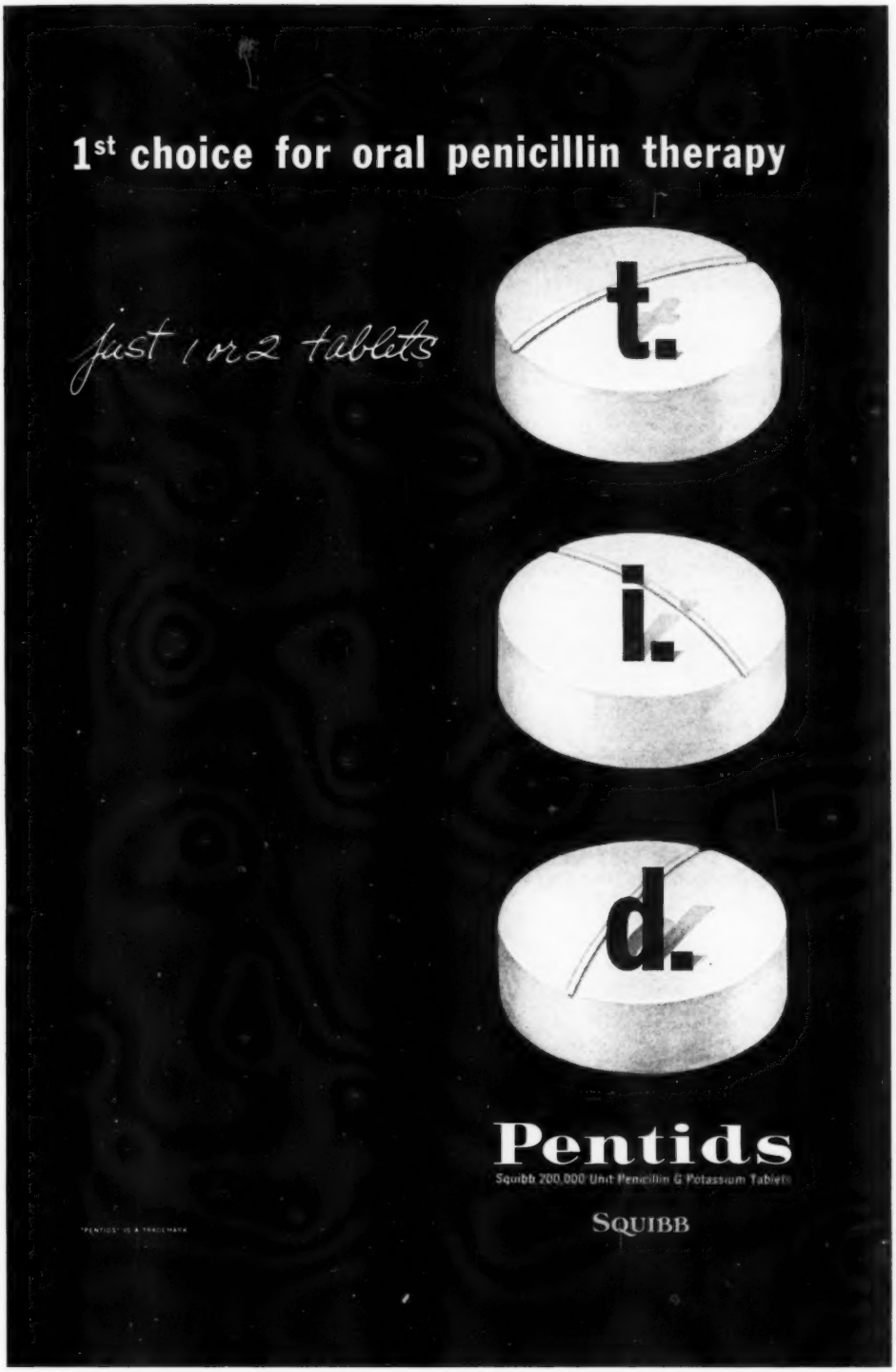
• AMNIONECTOMY IN UNRIPE CERVIX

Question: Given a patient who is full term with no apparent pelvic contraction, and in whom it is decided to induce labor by rupturing the membranes even though the cervix is not ripe: (It is realized that the cervix should be ripe before attempting an amnionectomy.) Is there room for criticism because a moderately difficult midforceps extraction resulted? Could this have been avoided by waiting until the cervix was ripe before rupturing the membranes? Or is it true that an amnionectomy in an unripe cervix had nothing to do with the delivery being a difficult midforceps?

M.D.—California

ANSWER: I would say that it is not considered good judgment in obstetrics to rupture the membranes prematurely, especially where there is some question in regard to the size of the cervix or when the cervix is not "ripe." I would say that the amnionectomy in an unripe cervix had something to do with the delivery being a difficult midforceps. I would not advise amnionectomy in this type of case.

(Continued on page A-40)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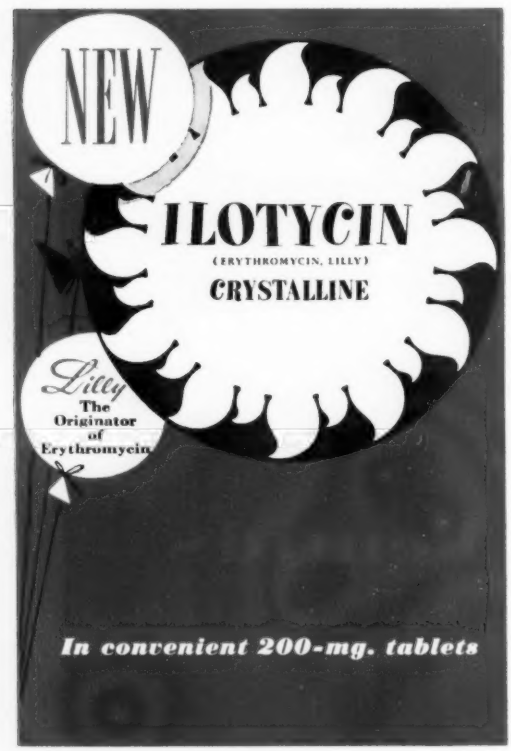
• REMOVAL OF SEBACEOUS CYSTS

Question: A woman with a somewhat oily skin who has had acne since adolescence now has many small sebaceous cysts, particularly around the mouth and chin. What are present views as to the manner by which these should be removed? Are there any remedies which may be included in ointments useful in such conditions? Some of my colleagues say that these are best removed one by one, using expression; others say x-ray treatments are most effective.

M.D.—Illinois

ANSWER: Little can be done in the treatment of oily skin with sebaceous cysts. Temporary removal of the oil can be done with application of acetone (10 per cent in alcohol). This is palliative, not curative. The cysts can be removed surgically, either by very light desiccation or with the scalpel. Careful expression of small sebaceous cysts is of no value as the cysts will soon refill. Also x-ray is contraindicated in the treatment of this condition.



Information for AUTHORS

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Galley proofs will be furnished the authors. Reprints of articles are available and a price list and order card are submitted with the galley proofs.

All correspondence pertaining to editorial matters should be addressed to the Editorial Department, POSTGRADUATE MEDICINE, Essex Building, Minneapolis 3, Minnesota.

The Place of Antihistaminics in the Treatment of Allergic Disorders

JOHN M. SHELDON*

University of Michigan Medical School, Ann Arbor

JOHN M. SHELDON

ABOUT 10 years ago the antihistamines were first called to our attention for use in allergic disease. Since that time there have been reports about the use of antihistamines in the treatment of about 125 different conditions or symptoms. It now seems timely to review and evaluate what this group of drugs can and cannot do.

First I would like to introduce a patient Dr. Hoerr was kind enough to send us from the Cleveland City Hospital. This gentleman is a 57 year old Negro who was in relatively good health until July 1951 when he experienced his first attack of shortness of breath. This occurred in a setting of severe anxiety about the welfare of his second wife, who was pregnant and suffering from pernicious vomiting. Since then the patient has never been well enough to work and has spent almost half his time in the hospital.

During a previous admission to the City Hospital it was found that every attack occurred during an emotionally charged period. Some attacks could be alleviated by simple psychotherapy. ACTH, cortisone, and the antihistaminic agents were ineffective.

The patient was again admitted two days ago to the Cleveland City Hospital in status asthmaticus.

It can be readily seen that the patient has a continuous respiratory effort. A point of paramount interest is that he has considerable congestion of his nose and gives a history of prolonged nasal stuffiness, the so-called "nasal stuffynositis."

The salient points of interest are these: the marked pulmonary emphysema; the very marked increase in anteroposterior diameter, and, as shown roentgenographically, the widening of the intercostal spaces and some flattening of the diaphragm out of proportion to what we might expect in an individual 57 years of age.

The important thing, so far as antihistamines are concerned in this case, is that they should have a certain degree of effectiveness in controlling the nasal inflammation the patient has had for many years.

From the standpoint of management of his asthma, repeated doses of antihistamines are definitely contraindicated because he has difficulty raising his sputum; all the antihista-

*Professor of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan.

Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association in Cleveland.

mines have an atropine effect which would increase this difficulty. However, it has been conclusively shown that a high percentage of patients in status asthmaticus will become ADRENALIN®-tolerant if you give them single, adequate doses of an antihistamine intravenously. Repeating the doses over periods of time, however, again thickens the bronchial secretions and increases the respiratory difficulty. Therefore, so far as an antihistamine is concerned, it has just one use and that is one dose intravenously, if it permits the patient to benefit from the administration of the Adrenalin.

To continue the physical findings and review of his chest x-rays, no great pathology is seen within the chest itself. We see only slight flattening of the diaphragm, so there is a reasonably good prognosis in his case. We do see some evidence of increased radiotranslucency and the intercostal spaces are definitely increased.

Pharmacologic Activity of Antihistamines

The antihistaminics have many pharmacologic activities, and for that reason their use has been suggested in a great number of conditions and situations. Their antihistaminic effect is one of the primary reasons for their use in cases of anaphylactic reactions or severe allergic shock and is why they are effective in such conditions as urticaria, angioneurotic edema and hay fever. They are all anti-anaphylactic and anti-allergic. They will protect an animal against histamine shock; as a matter of fact most of them will protect against several times the lethal dose that kills an animal. They are all sedative in action, and I am sure that some of the benefits reported, and that you have all seen, are entirely related to the sedative action. They all have atropine-like activity, some more than others, which I propose to discuss later. They all have some local anesthetic activity and are used for such things as preoperative bronchoscopy, etc. They are also anti-emetic, and here again certain of them are more effective than others. Apparently they all have an effect on the enzyme system and an antihyaluronidase effect, which is particularly useful in dealing with such things as contact dermatitis and atopic eczema.

Chemical Groups

From the practical viewpoint there are now some 26 antihistaminic agents on the market. Is there any justification for all of these? I think there is, because one can divide these antihistamines into various groups and, from each, select a particular drug for the condition one wishes to treat. I don't wish to remember 26 different drugs for administration in patients with hay fever, but I am interested in remembering representatives from four separate groups. Any one of the four groups will be clinically applicable in any given instance.

Chemically speaking, if we hook the phenolic rings onto a carbon chain through an oxygen linkage, we know that the antihistaminic activity is about second so far as groups are concerned, and the toxicity is No. 1 (by toxicity I mean the side effects produced, such as drowsiness). If we take a second group in which the phenolic rings are hooked onto the carbon chain through a nitrogen linkage, the antihistaminic activity is No. 1 and the toxicity is No. 2. A drug of this group is less likely to make your patient drowsy or to produce gastrointestinal or other symptoms. In a third group, in which the phenolic rings are hooked onto the carbon chain through a CH_2 linkage, the drugs are less protective so far as antihistaminic action is concerned, less likely to produce toxicity, and less likely to make your patient sleepy.

If you have a patient who has hay fever and who is working in a bank, and you want to give him relief of symptoms, obviously you would select a drug from the third group or from still a fourth group, injection of which is less likely to cause drowsiness.

Good examples of group 1 are BENADRYL®, DECAPRYN®, DRAMAMINE® and HYDRYLLIN®. This particular group tends to produce drowsiness, and would be used for a patient who has serum sickness or acute urticaria, for example, who has not rested well and in whom you want sedative action. Furthermore,

pharmacologically speaking, this group is very much more likely to have an anti-emetic effect, and if you want an antihistamine to reduce the likelihood of seasickness or motion sickness, you would pick one from this group. On the other hand, if you do not wish the patient to have the side effects of drowsiness, you would certainly not select one of these compounds.

Examples of the second group are NEOANTERGAN®, NEOHETRAMINE®, PYRIBENZAMINE®, PYRROLAZOTE®, HISTADYL® and THENFADIL®. These products have greater activity so far as the enzyme action and the antihyaluronidase action are concerned. If you have a patient who has contact dermatitis or atopic eczema, you might choose a drug from this group, especially if the individual has a contact dermatitis of the lids. For example, in patients who have atropine sensitivity and in whom you still wish to introduce the atropine for its mydriatic effect, you might instill a compound in the eye from this group before using atropine and expect greatest benefit so far as the antihistamines are concerned.

Examples from the third group are CHLORTRIMETON®, and TRIMETON®. If you have a patient for whom you want less sedative action, but still good antihistaminic action—say, a patient wtih hay fever—you might use a drug from this group. THEPHORIN® and ANTISTINE® are less likely to produce drowsiness; as a matter of fact, they frequently produce the opposite effect.

Indications for Use of Antihistamines

I am not going to name all the conditions in which the antihistamines are used, but I will discuss those of more prominence numerically and from the standpoint of the use of the drugs.

Antihistamines will relieve certain symptoms of seasonal hay fever. If the individual has sneezing, rhinorrhea and itching of the nose and eyes and redness of the eyes, in about 80 per cent of instances those symptoms will be controlled by adequate doses of an antihistamine. On the other hand, if the primary symptom in hay fever is that of nasal obstruction, an antihistamine won't be of any benefit. It is to those patients that you give acetylsalicylic acid if they are not sensitive to it. The antihistamines are not the whole answer for seasonal hay fever, however, because you are treating the symptoms only; once you stop the drug the symptoms will return. Furthermore, Brighton in England has quite well demonstrated, I believe, that there is greater incidence of development of asthma following hay fever in those patients who have been given antihistaminics alone. If you treat the patients with the specific pollen extracts to which they are sensitive and then use the antihistamines, they will not develop seasonal asthma. Furthermore, your results rise to about 95 per cent.

Results are equally effective in perennial allergic rhinitis, as in seasonal hay fever. Again, I should like to emphasize that if edema of the nasal mucous membrane and turbinates is the primary symptom in the patient, the antihistamines are not the answer; you must resort to something else, such as aspirin. But the antihistamines will control the other symptoms, namely, rhinorrhea, sneezing, itching of the nose and eyes and ears, and so forth.

In bronchial asthma, the patient previously presented illustrates the primary considerations. Certainly for status asthmaticus—other than the one dose given intravenously—the drugs are actually contraindicated. However, in children or in individuals having mild asthma, they are of some use in aborting or preventing occurrence of attacks. One must carefully evaluate clinically every asthmatic patient before prescribing an antihistamine.

The antihistaminics are very effective in urticaria, particularly in the urticaria related to serum sickness from penicillin, delayed serum sickness reaction, food and drugs. However, there are two or three clinical points I should like to emphasize: In case of serum sickness, it is important to use the antihistamine early. If the patient has not had therapy for 24 or 48 hours after the onset of the serum sickness, he is unlikely to receive satisfactory benefit with an antihistamine. Itching will perhaps be somewhat relieved, but the disease will continue much as though you had not

given the antihistamine. Therefore, it is important that an antihistamine be given early and in adequate doses.

If symptoms are progressing very rapidly, it is worth while to consider seriously giving the first dose of the antihistamine intravenously and then repeating it every 4 to 6 to 12 hours, depending on what antihistamine you are using, for a period of at least 3 days after all signs and symptoms have disappeared.

One other practical consideration is that for Patient *A* antihistamine *A* from group 1 may be effective; however, for Patient *B* antihistamine *A* may not do a thing. We don't know why, but that is a clinical observation. But Patient *B* may have dramatic relief with antihistamine *B* from group 2. If he doesn't have relief with the second group of compounds, he may with the third; if he doesn't have it from the third, he may from the miscellaneous or fourth group. In general, this is true of the other conditions previously mentioned; however, it is more important to go rapidly from one group to another in case of serum sickness for the reasons already stated.

In cases of drug sensitivity of the eyes, there is great need in certain instances to use atropine or atropine compounds to dilate the pupils, and the incidence of atropine sensitivity is relatively high. Local reactions may be reduced by instilling an antihistamine into the eye. In such cases we frequently use Antistine for reasons already mentioned, although others may be used as well. At the same time we prescribe an antihistamine to be taken orally. It will not completely obliterate the local drug sensitivity reaction to compounds such as atropine, but, in most instances, it will reduce the subjective symptoms so that the drug may be continued indefinitely.

The antihistamines may also be used in other instances of drug sensitivity. They have been recommended as a means of preventing penicillin reactions. The information to date, to my mind, is not conclusive, and I think that one should use antihistamines in connection with pre-penicillin administration or simultaneously with penicillin with considerable mental reservation. I am convinced that studies reported to date have not been adequately controlled, although they do look rather promising.

In regard to dermatoses, particularly atopic eczema, there are two points I wish to emphasize here: (1) The antihistamines are effective only in relation to control of the pruritus, but they do not influence the course of the disease at all. (2) I plead against the topical use of antihistamines in atopic eczema, and in general of any skin disease, with perhaps the exception of pruritus ani and pruritus vulvae where in certain instances topical applications may be definitely indicated. I think the drugs are contraindicated because their effect is very transitory and is entirely related to the inherent local anesthetic action of the antihistamine. It is a profound but transitory effect. Secondly, the incidence of induction of contact sensitivity is great following topical administration. Lastly, exactly the same result, without complications, can be accomplished by oral administration of the antihistamine.

The antihistamines are of some use not only in atopic eczema but also in contact dermatitis or dermatitis characterized by itching. The drugs will not cure the patient but they will reduce the itching and make your patient much more comfortable. Here again, I want to emphasize that you must use adequate dosages. The dosage depends on the size of the person, on the individual tolerance, and on the antihistamine selected. In general, for most antihistamines, the dosage is 50 mg. every 4 hours. There are antihistamines that are effective for much longer periods, and there are antihistamines that require much smaller doses. For example, the average dose of Chlor-Trimeton is 4 mg., although many patients require 10 mg., and even though the average dosage of Pyribenzamine may be 50 mg. every 4 hours, certain patients require 100 mg. every 4 hours. One should use the therapeutic dosage and it varies from patient to patient. If there are no side reactions with a given dose and the therapeutic effect is not as great as you desire, you are perfectly justified in increasing the dose.

In case of migrainous headache, it is extremely doubtful, in my opinion, that anti-

histamines are of any great use. Those patients who have been helped, I am sure, have received the benefit of the sedative effect of these compounds.

So far as gastrointestinal allergy is concerned, the antihistamines will prevent the usual symptoms associated with a food sensitivity if they are given before the patient ingests that particular food. They won't relieve all patients, and I should like to warn you in this respect. If you have a patient who eats lobster and has nausea, vomiting and diarrhea, and urticaria, I suggest that you do not give him an antihistamine a half hour before his meal and say, "Go on and eat your lobster," because he will have some degree of symptoms anyway. But for the milder symptoms related to gastrointestinal allergy and against those foods that are less explosive than the seafoods, the drugs may be very helpful—particularly for milk, wheat, and that group of foods.

The antihistamines are very useful in physical allergy. This concerns a very small number of patients, however, but the drugs will really control the urticaria due to cold or heat, for example, and they will lessen the allergic reaction to sunlight, although they won't completely obliterate it. In this particular instance, one should use an antihistamine having the greatest antihyaluronidase effect, and that is a compound from group 2 of which Pyribenzamine and Neohetramine are members.

As to the common cold, I believe the antihistamines neither prevent nor shorten the duration of this complaint. They may make the patient feel better because they have an atropine effect and lessen the nasal secretions. They may be beneficial because they all have a sedative action and the patient gets more rest and more sleep, but they neither prevent nor cure the common cold.

Antihistamines will lessen the itching of measles and I think are indicated in that disease. They are also of value in chickenpox. They are of help in stopping cough, regardless of cause, and gargling with an antihistamine is very effective in relieving a sore throat. A favorite method of mine is to order 15 cc. of an elixir of an antihistamine and 15 cc. of water which the patient may mix himself and use as a gargle every 3 or 4 hours. It is of use because it has a local anesthetic effect.

In motion sickness, the antihistamines are useful, and I would select compounds from group 1, such as Decapryn, Benadryl or Dramamine.

In summary, the antihistamines are useful agents when it is recognized what they will do and what they won't do. One may use various groups of antihistamines for certain types of symptoms because of their wide pharmacologic action. Finally, I would like to urge that you use adequate doses of antihistamines, chosen from various groups in the event that your patient does not obtain symptomatic control with drugs from the original group selected.

MEETINGS AND POSTGRADUATE COURSES

AAAS Conference on Scientific Editorial Problems: The conference session will be held at the Mechanics Building in Boston on Sunday evening, December 27, 1953, in conjunction with the annual meeting of the American Association for the Advancement of Science.

American College of Chest Physicians: Second regional postgraduate course on diseases of the chest, February 15-19, 1954, at New Orleans and the seventh annual postgraduate course on diseases of the chest, March 15-19, 1954, at the Bellevue Stratford Hotel, Philadelphia. Tuition for each course is $75. Further information may be obtained from the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

University of Minnesota, Minneapolis: Continuation course in neurology for general physicians and specialists, January 25-30, 1954, at the Center for Continuation Study. Diagnosis and management of the more commonly met neurologic disorders will be stressed. The annual John B. Johnston Lecture will be presented on the evening of January 27 by Dr. Andrew T. Rasmussen, Professor Emeritus of Anatomy, University of Minnesota Medical School. Course will be presented under the direction of Dr. A. B. Baker, Professor and Director of Neurology, who will be joined by other members of the University of Minnesota Medical School and the Mayo Foundation, along with guest faculty from Utah, Kansas and Iowa.

Metastatic Manifestations as Presenting Symptoms of Primary Cancer of the Lung

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Analysis is made of 2000 cases of primary cancer of the lung. In more than 10 per cent, the first symptoms were due to metastases, most commonly to bone and brain. The lack of symptoms of early cancer of the lung is emphasized, and the importance of searching for peripheral nodes either in the presence of known lung cancer or to establish the diagnosis is pointed out. The necessity for surveys to detect early lung cancer, when a high cure rate is possible, is stressed, and the need for exploratory thoracotomy in a suspicious lesion when other diagnostic measures fail is noted.

It has long been known that the first symptoms of primary cancer of the lung may be due to metastases. This was noted by Adler[1] in his exhaustive monograph published in 1912. One such case cited by him had been reported in 1871. Various other observers have also called attention to this fact, among them Fried[2] in 1925, Miller and Jones[3] in 1930, Rogers[4] in 1932, Jaffe[5] in 1935, Ochsner and DeBakey[6] in 1942 and Björk[7] in 1947. The present study was undertaken because we were impressed by several striking instances of this character and wished to determine if there was a significant incidence of such cases in a large series.

Our material consisted of 2000 cases diagnosed as primary cancer of the lung at Hines Hospital from January 1, 1931 (when the research tumor statistic section was organized) to March 31, 1952. It should be noted that less than 1 per cent of the admissions at Hines are women, and no children are admitted. Only 1 of the 2000 patients was a woman.

Table 1 indicates the basis for the diagnosis in each case. In this tabulation, where both biopsy and autopsy were positive, only the autopsy was listed; where biopsy of both the primary and the metastatic lesions was positive, only the primary biopsy was recorded. Of the 447 cases without any pathologic confirmation, there were 10 with equivocal primary and 2 with equivocal metastatic biopsies. Many of the remaining 435 cases had negative biopsies. The rest (about half of the 435) had no biopsy for one reason or another—e.g., some patients refused permission for biopsy, in some no material for biopsy could be obtained, and others were terminal.

TABLE 1

BASIS FOR DIAGNOSIS OF PRIMARY CANCER OF THE LUNG (2000 CASES)

Autopsy	851
Biopsy of primary lesion	503
Biopsy of metastases	199
X-ray and/or clinical evidence of cancer	447
	2000

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Bone Metastases

First the bone metastases were analyzed. There were 346 in all. These were divided into 2 general groups: A, in which the bone lesions were established by autopsy or biopsy, and B, in which the bone lesions were demonstrated only by x-ray with or without clinical findings. However, in this group the presence of cancer was confirmed by autopsy or biopsy in all but 46 cases. The cases in which the bone metastases gave rise to the presenting symptoms were similarly subdivided and the results listed (Table 2).

There were 3 additional autopsies demonstrating primary cancer of the lung in which cancer of the bone was proved by biopsy but the bones were not examined at autopsy.

Incidence—Thus, the 346 bone metastases constituted 17.3 per cent of our 2000 cases, or 13.8 per cent of 1,553 if only the bone metastases proved by autopsy or biopsy are included and all other cases with only x-ray findings omitted. There is considerable variation in the percentage of bone metastases recorded in the literature; for example, Adler[1] reported 15 per cent of 374 cases, Ochsner and DeBakey[6] 21.3 per cent of 3,047, Björk[7] 6.8 per cent of 234, Hubeny and Mass[8] 24 per cent of 150 and Abrams[9] 32.5 per cent of 160. These figures necessarily vary because of a number of factors such as the stage of the disease and the thoroughness of the autopsy.

The highest incidence in the group just cited was obtained by Abrams,[9] who made routine sections of the dorsal and lumbar spine in all his 160 cases. It is generally conceded that the actual occurrence of bone metastases from primary cancer of the lung is considerably greater because radiography fails to demonstrate all the bone lesions and the skeleton is not examined routinely at autopsy. This point was well brought out by Snure and Maner,[10] who described a case in which only a lesion of L_5 was found radiographically but most of the vertebrae were found to be involved at autopsy. (We have had a similar experience in plasma cell myeloma—only a lesion of D_{12} on x-ray but all the lumbar vertebrae involved at autopsy.) Snure and Maner[10] subsequently demonstrated that practically all the spongiosa of a vertebral body can be replaced without demonstrable x-ray signs. They state that at least 1 sq. cm. of cortex must be destroyed before a difference in density can be shown radiographically. According to Borak,[11] a lesion in the body of a vertebra becomes visible radiographically only in the advanced stages, while a defect which changes contour may be seen relatively early. He points out that metastatic bone lesions may be present on x-ray without clinical findings or may cause symptoms without radiographic evidence. A good example of bone symptoms present long before a destructive lesion was evident radiographically is Case 3, described in detail later.

TABLE 2

SUMMARY OF BONE METASTASES IN 2000 CASES OF PRIMARY LUNG CANCER

	ALL BONE METASTASES	PRESENTING SYMPTOMS OF BONE METASTASES
Group A		
Diagnosis based on		
Autopsy	184	34
Bone biopsy	30	10
Group B		
Diagnosis based on		
Autopsy excluding bone	25	4
Biopsy of primary lesion	44	4
Biopsy of other metastases	17	3
X-ray and/or clinical evidence of cancer	46	15
	346	70

TABLE 3

DISTRIBUTION OF BONE LESIONS (346 CASES) *

Ribs		178
Spine		179
Dorsal	59	
Lumbar	57	
Dorsal, lumbar	25	
"Entire spine"	5	
"Vertebrae"	17	
Cervical	4	
Cervical, dorsal	5	
Lumbosacral	2	
Sacral	5	
Pelvis (ilium, 22)		38
Femur		26
Skull		25
Clavicle		18
Scapula		13
Sternum		9
Humerus		6
Tibia		2
Maxilla, mandible, radius and metacarpal		1 each

*In many cases there were metastases to more than one bone.

TABLE 4

RELATIVE FREQUENCY OF BONE METASTASES FROM OTHER MALIGNANCIES AND OF PRIMARY BONE TUMORS

PRIMARY MALIGNANCY	NUMBER OF CASES	BONE METASTASES	
		Number	*Per Cent*
Prostate	704	284	40
Kidney	383	84	21.9
Thyroid	94	16	17
Hodgkin's disease	566	41	7.2
Miscellaneous		100	
PRIMARY MALIGNANT BONE TUMORS			
Sarcoma			121
Myeloma			88
Ewing's			20
Other malignancies			21
			250

Distribution—Any bone may be attacked. In our series the ribs and the spine were most often affected (Table 3). Even the phalanges may be involved. Colson and Willcox[12] reported 2 cases with involvement of phalanges of the fingers; in 1 of these the third metatarsal was also affected, and in a third case there was metastasis to the left first metatarsal.

Types of bone lesions—There were 5 osteoblastic metastases, 4 to the spine and 1 to a rib. One of these is described in the case reports. All the rest were osteolytic.

To get a general idea of the relative frequency of bone metastases from other malignancies and also of the relative frequency of primary bone tumors (during the period of this study), the data listed in Table 4 were obtained from the research tumor statistic service (but were not analyzed in detail). From these data it can be seen that at Hines Hospital the bone metastases from bronchogenic carcinoma were more numerous than all the primary malignant bone tumors or than the metastases from all other metastatic malignancies excluding cancer of the prostate. Further, in an adult male, a malignant osteolytic bone lesion, especially of the ribs or spine, is much more apt to be secondary to cancer of the lung than to any other neoplasm. (However, nonmalignant bone lesions may represent quite a problem in differential diagnosis, especially with a combination of bone and lung involvement as in tuberculosis.

Brain Metastases

The next group consisted of 218 brain metastases. These were divided into 2 main groups similar to the bone cases: group A in which the brain lesion was established by autopsy or biopsy, and group B in which only clinical findings of brain involvement were present but cancer was demonstrated pathologically in all but 52; in these 52, there was x-ray evidence of cancer of the lung with or without clinical findings (Table 5).

Incidence—The incidence of brain metastases in our entire series was 10.9 per cent, but if only the cases confirmed pathologically are included, the percentage is 6.6 (103 in 1,553). The statistics given in the literature on this point vary considerably; for example, 39.4 per cent in 38 cases reported by Fried and Buckley,[13] 9.5 per cent of 808 cases by Miller and Jones,[3] 16.5 per cent in 3,047 collected cases by Ochsner and DeBakey,[6] and 4.7 per cent of 234 proved cases by Björk.[7] It appears reasonable to assume that a higher percentage would have been obtained in our series if the brain had been examined at autopsy in all the remaining brain cases; an

TABLE 5

SUMMARY OF BRAIN METASTASES IN 2000 CASES OF PRIMARY LUNG CANCER

	ALL BRAIN METASTASES	PRESENTING SYMPTOM OF BRAIN METASTASES
Group A		
Diagnosis based on		
Autopsy	98	37
Brain biopsy	5	4
Group B		
Diagnosis based on		
Autopsy excluding brain	18	3
Biopsy of primary lesion	31	4
Biopsy of other metastases	14	4
X-ray and/or clinical evidence of cancer	52	13
	218	65

TABLE 6

PERIPHERAL LYMPH NODE INVOLVEMENT IN 2000 CASES OF PRIMARY LUNG CANCER

TYPE OF NODE	NUMBER OF CASES
Supraclavicular	145
Cervical	110
Axillary	32
Supraclavicular and cervical	14
Supraclavicular and axillary	11
Cervical and axillary	12
Axillary and inguinal	1
Cervical and inguinal	5
Inguinal	3
	333

even higher incidence could be expected if the brain were examined at autopsy in all persons dying of cancer of the lung, as brain metastases may be silent. The clinical significance of metastases of the brain has been stressed by a number of observers. One of the earliest instances of this type—included in Adler's[1] series—was first reported in 1871. Fried[14] and Parker[15] have called particular attention to this point. Fried and Buckley[13] found that in 11 out of 15 instances of metastatic carcinoma of the brain, the primary lesion was overlooked. Craig, Woltman and Kernohan[16] stated that they obtain routine films of the chest in all cases in which tumor of the brain is suspected. Even when there are symptoms of primary tumor, the signs of brain involvement may dominate the clinical picture.

During the period of this study, a diagnosis of primary brain tumor was made at Hines Hospital in 989 cases. These included 267 not determined histologically and 144 pituitary tumors (not necessarily established by microscopic examination). These figures were obtained from the research tumor statistic service without further attempt at breakdown. (The statistics for other metastatic brain tumors were not available at the time of this report.) The problem of differentiating a primary from a secondary pituitary tumor would seldom arise, since the pituitary is rarely involved by metastasis from primary cancer of the lung. Adler[1] reported only 1 such case and there were 2 in our series, and these patients did not have symptoms of pituitary involvement. If one then omits the 144 pituitary tumor cases and considers only proved brain tumors, there is approximately 1 secondary to cancer of the lung to 6 primary brain tumors. If all the cases diagnosed as primary brain tumor except these 144 are included and compared with our entire group of 218, then the ratio becomes approximately 1 to 4. This emphasizes again the necessity for examining the chest radiographically when a neoplasm of the brain is suspected.

Peripheral Lymph Node Metastases

There were 333 cases with involvement of peripheral nodes. In 306 of these, the diagnosis was confirmed by autopsy or biopsy. In the remaining 27, the lesions of the nodes were only found clinically, but there was also evidence of primary cancer of the lung radiographically with or without clinical findings. The total distribution is listed in Table 6.

Thus the incidence of lymph node involvement was 16.6 per cent of the 2000 cases, or 19.7 per cent (306 in 1,553) if only the cases confirmed by autopsy or biopsy are included. Of the 1,553 cases, there were 131 or 8.4 per cent supraclavicular nodes, 101 or 6.5 per cent cervical, and 31 or 2 per cent axillary. Ochsner and DeBakey,[6] in their com-

prehensive study of metastases from cancer of the lung, gave the following figures based on 1,298 cases: cervical 17.4 per cent, axillary 6.6 per cent and supraclavicular 4.2 per cent. Björk[7] found 10.7 per cent cervical, 9.0 per cent supraclavicular and 4.3 per cent axillary in 234 proved cases. Björk[7] emphasizes that the lymph node metastases occur far more frequently on the same side as the primary tumor than on the other side but may be present bilaterally. The importance of these peripheral metastases as an aid in establishing the diagnosis as well as in modifying the treatment of primary cancer of the lung has been stressed by Ochsner and DeBakey.[6]

Miscellaneous Metastases

This group consisted of 82 cases with a variety of presenting symptoms. The basis for the diagnosis of cancer in these cases is given in Table 7. Thirty-four of these patients had symptoms referable to the abdomen or gastrointestinal tract. Twenty-two presented metastatic peripheral nodes. The remainder included an assorted group—masses in the skin, swelling of the face, and evidence of cord tumor. Of the 22 with metastatic peripheral nodes, 19 were cervical or supraclavicular, 2 were axillary and 1 inguinal; in 18 of these, the diagnosis was made by biopsy of the affected node. It is noteworthy that in 131 or 8.4 per cent of the 1,553 cases confirmed by autopsy or biopsy, the initial (and often the only) histologic proof of cancer was afforded by biopsy of the involved nodes.

Finally, there were 2 small groups of cases which seemed to warrant inclusion. First, there were 15 cases with presenting symptoms unrelated to the primary tumor; in 8 of these, the diagnosis was confirmed by autopsy, in 3 by biopsy of the primary lesion, and in 1 by biopsy of a metastasis. One of these patients had resection of the prostate for carcinoma; later, primary cancer of the lung was confirmed by biopsy. Another had resection of the stomach for cancer and subsequently pneumonectomy for cancer of the lung. One of the most striking of this group was a patient admitted because of a cerebrovascular accident who was found to have a pituitary tumor by x-ray and clinical study. Autopsy disclosed multiple cerebral thromboses with cerebral softening, an eosinophilic adenoma of the pituitary, and a totally unsuspected 10 cm. primary cancer of the lung.

TABLE 7

DIAGNOSIS OF MISCELLANEOUS METASTASES IN 2000 CASES OF PRIMARY LUNG CANCER

Autopsy	55
Biopsy of primary lesion	3
Biopsy of metastasis	11
X-ray and/or clinical findings	13
	82

The second group consisted of only 4 cases detected on a chest survey elsewhere. In these the diagnosis was confirmed by autopsy in 2, by biopsy of the primary lesion in 1, and by biopsy of the metastatic lesion in 1.

Case Reports

Case 1—A 26 year old white man was admitted December 28, 1944, complaining of pain in the left thigh of 4 or 5 months' duration; the pain had become progressively more severe until it was continuous. Then a mass appeared in his left groin, and this became larger. Weakness developed and he lost 15 pounds in weight. Physical examination revealed a painful mass over the crest of the left ilium. Roentgenograms showed a destructive lesion of the left upper ilium laterally, a similar lesion of the left sixth rib, and a small mass above the left hilum (Figure 1a and b). Biopsy of the mass over the left ilium demonstrated undifferentiated metastatic carcinoma. He was given x-ray therapy to the left pelvis with relief of pain but went progressively downhill and died March 31, 1945. At autopsy there was undifferentiated carcinoma of the left upper lobe with metastases to the mediastinal and abdominal lymph nodes and in the left sixth rib. (Complete autopsy was not permitted.)

Case 2—A 47 year old white man was admitted March 8, 1950, because of progressive pain in the left shoulder anteriorly, radiating to the elbow; weakness of the left arm had been noticed since December 1949. Also, there had been a small lump in the left axilla

Case 1.

FIGURE 1a

FIGURE 1b

for about 2 months, epigastric pain one-half hour after meals relieved or prevented by aspirin, and increased constipation. Physical examination disclosed weakness of the left arm, decreased motion of the left shoulder, pain on sudden motion of the left arm, a 3 cm. firm, movable node in the left axilla, a poorly defined mass in the posterior axillary fold, and a small, firm, movable subcutaneous nodule in the right upper quadrant. X-ray revealed an infiltrating lesion at the upper border of the right hilum and a destructive lesion of the glenoid process of the left scapula (Figure 2a and b). On biopsy of the subcutaneous nodule in the right upper quadrant, anaplastic carcinoma was found. Bronchoscopy showed blunting of the carina, but only chronic inflammatory tissue was demonstrated on biopsy from this region. X-ray therapy was given but the patient became progressively worse and died on July 20, 1950. The autopsy findings were anaplastic carcinoma of the right upper lobe and metastases to the mediastinal and hilum lymph nodes, both adrenals, pancreas, kidneys, liver and skin.

Case 3—A 56 year old white man was admitted October 12, 1948, complaining of numbness and tingling of the right thigh for 9 months, low back pain for 4½ months, weakness of the right leg for 4 months, loss of 10 to 11 pounds in weight and a slight cough for 2 months. Physical examination revealed marked tenderness to percussion over L_{-1}, positive Laségue's and Patrick's signs on

Case 2.

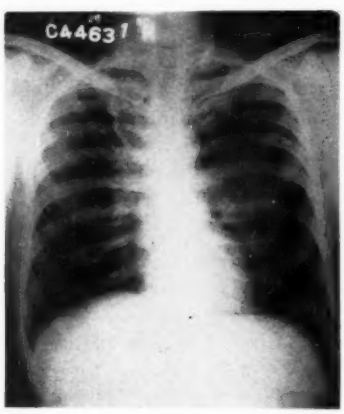

FIGURE 2a

FIGURE 2b

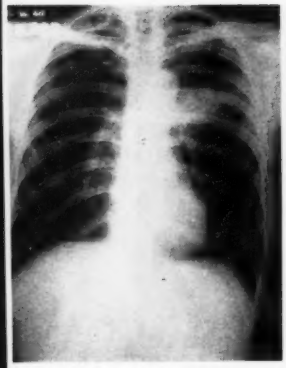

FIGURE 3a

FIGURE 3b

FIGURE 3c

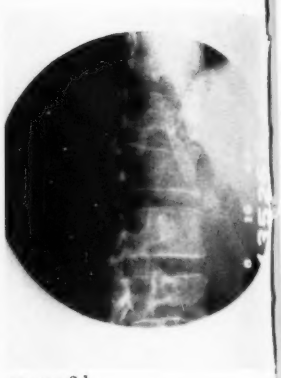

FIGURE 3d

Case 3.

the right, hypalgesia in the right L_{-1} dermatome, absent ankle jerks and diminished right abdominal reflexes. Radiographic examination of the lumbar spine was negative, but a mass adjacent to the left hilum was found on a routine chest film (Figure 3a and b). On November 3, 1948, a left pneumonectomy was performed; histologic examination demonstrated squamous cell carcinoma of the left upper lobe but no metastasis in the hilum nodes.

The patient made an uneventful postoperative recovery and was discharged on December 16, 1948. He was readmitted on June 14, 1949, because of severe pain in the lumbar region radiating down the backs of the lower extremities. Radiographic examination of the spine now demonstrated a marked destructive lesion of L_{-1} chiefly on the right (Figure 3c and d). He was given x-ray therapy with relief of the pain in the back and lower extremities. He was discharged on August 31, 1949, but returned in a short time because of severe pain in the lumbar area. He now had numbness and sensation of needles and pins in both thighs anteriorly and a moderate cough. He was given palliative radiation with only slight relief. He died on January 9, 1950. At autopsy no recurrence of the carcinoma was found in the chest, but there was tuberculosis of the right lung and right ventricular hypertrophy with right heart failure.

Case 4—A 23 year old Negro man was admitted May 24, 1948, because of sacroiliac pain, belching, and a loss of 10 to 15 pounds in weight in 3 months. Physical examination revealed a 2 cm. mass in the right cervical region, moderately enlarged glands in both axillas, dullness and harsh breath sounds in the upper third of the right lung, and an immobile lumbar spine. Radiographic examination revealed masses extending above and below the right hilum with a few strands radiating from these masses, elevation of the right diaphragm, and osteoblastic lesions of D_{-12} and L_{-1} (Figure 4a, b and c). On May 29, paralysis of the lower extremities suddenly developed and he lost voluntary control of urination and defecation. By May 31 he had complete flaccid paraplegia with a sensory level of L_{-1} or L_{-2}. On June 4 a decompressive laminectomy was done and tumor tissue removed extradurally, chiefly anterior and lateral to the cord from D_{-9} to D_{-11}. Histologic report of this tissue was lymphoblastoma (the radiographic and clinical findings were certainly compatible with this diagnosis). He was given x-ray therapy to the right chest and lumbar regions with considerable improvement clinically as well as clearing of the pulmonary lesion. He began to regain function of the lower extremities, bowel and bladder. Then he was given x-ray therapy to the right cervical region but following this became progressively worse and died on February 20, 1949. Autopsy disclosed anaplastic carcinoma of the right lung with metastases to the medi-

Case 4.

FIGURE 4a

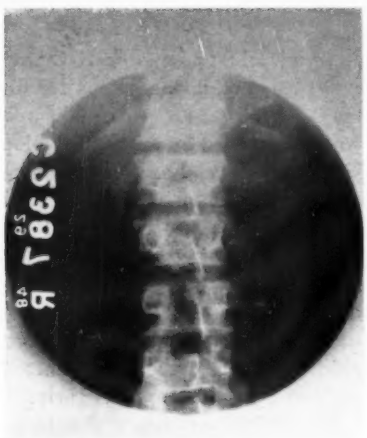

FIGURE 4b

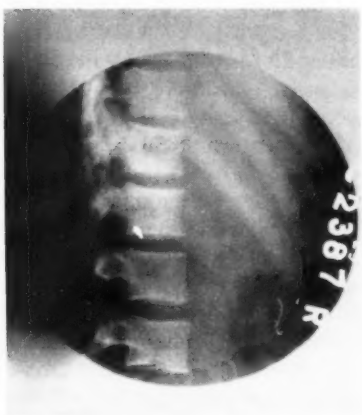

FIGURE 4c

astinal, periaortic and mesenteric nodes, pancreas, liver, D_{-12} and L_{-1}, and the right third rib. On review of the original slides at this time, the lesion was also found to be anaplastic carcinoma (and not lymphoblastoma).

Case 5—A 50 year old white man was admitted on June 27, 1950, with the following history: an episode of difficulty in speaking and writing on April 6, 1950; on April 13, 1950, an attack of syncope while at work, and on April 29, 1950, a convulsion involving the right side of the face and body, followed by aphasia for several hours. On May 6, 1950, he entered a private hospital where a left-sided mass was found on pneumoencephalography. At surgery, there was an "abscess" cavity at the junction of the middle and lower thirds of the precentral gyrus. Fluid from this cavity was sterile on culture, but penicillin and THOROTRAST® were put into the cavity at operation. The patient was discharged on May 22, 1950, but returned on June 5 because of recurrent seizures. On June 6, 20 cc. of purulent material and some clear brownish fluid were removed from the cavity in the brain, but again no organisms were present on culture.

On admission to Hines Hospital, the patient had right hemiplegia and aphasia but no papilledema. An admission chest film revealed a small infiltrating lesion of the left upper lobe and a destructive lesion of the left clavicle which were interpreted as probably inflammatory (Figure 5a). On June 30, 1950, the patient was taken to surgery because it was felt that further drainage was indicated, but only cerebritis was found in the left frontal area. On July 8, a slight hemoptysis occurred, and

FIGURE 5a

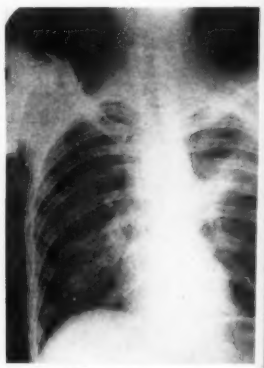

FIGURE 5b

Case 5.

another x-ray of the chest (Figure 5b) revealed the lesion in the left lung to be larger. Aspiration biopsy of the clavicular lesion failed to demonstrate tumor cells. The patient became progressively worse and died on July 27, 1950. Autopsy disclosed anaplastic carcinoma of the left upper lobe with metastases to the mediastinal, hilum and aortic lymph nodes, brain and liver. Other findings were thrombosis of the left subclavian vein, left renal infarct, mitral disease and generalized arteriosclerosis.

Case 6—A 55 year old white man was admitted April 12, 1950, with history of confusion, headaches and numbness of the left leg for a month; one week before admission, a puslike discharge from the right nostril began and the mental state "cleared up" but soon recurred. On admission, he was stuporous and weak, and the history had to be obtained from his wife. Neurologic examination revealed bilateral papilledema; hyperactive deep reflexes, more pronounced on the left, and bilateral Babinski. Spinal fluid was under increased pressure and contained 130 mg. protein. X-ray of the chest (Figure 6) revealed a small mass at the left hilum. Bronchoscopy was negative. He gradually became more stuporous and died on May 16, 1950. Autopsy disclosed an undifferentiated carcinoma of the left lung with metastases to the right frontal lobe, thyroid, cervical, regional and mesenteric lymph nodes.

Case 7—A 60 year old white man was admitted May 18, 1951, complaining of mild epigastric cramps of 3 weeks' duration occurring half an hour after meals and relieved by soda but not by food, and loss of 18 pounds in weight. Physical examination revealed cardiac enlargement, an occasional extrasystole, deep epigastric tenderness, the liver edge palpable at the costal margin, and a right supraclavicular node. Blood examination showed 3,300,000 red blood cells and 10.5 gm. hemoglobin. Radiographic examination of the chest revealed an infiltrating lesion of the right middle lobe (Figure 7a and b). Bronchoscopy demonstrated a fungating mass in the right middle lobe bronchus which proved to be anaplastic carcinoma on biopsy. The patient was given x-ray therapy to the chest (with some regression) and, later, nitrogen mustard. He was discharged on August 14, 1951, but soon had to be readmitted because of cord involvement. X-ray therapy relieved the sacral pain somewhat. The patient's condition deteriorated and he died on November 1, 1951. Autopsy disclosed anaplastic carcinoma of the right middle lobe bronchus with metastases to the pancreas, liver and adrenals.

Discussion

In all, 217 patients or 10.8 per cent of the 2000 had presenting symptoms due to metastases—173 or 11.1 per cent if only the 1,553 cases confirmed by autopsy or biopsy are considered. In 19 other cases there were no pulmonary symptoms. Furthermore, in a significant number of the cases we have counted as having presenting symptoms due to the pulmonary lesion, the complaints were actually due to extension of the disease to the chest wall or to the mediastinum. It seems reasonable to assume, therefore, that these latter patients had no symptoms early.

In 1925 Fried[3] stated that in primary cancer of the lung, symptoms may be latent due to metastases or to cancer in general. Rogers[4] reported 44 per cent of 50 autopsy cases and Jaffe[5] 20 per cent of 100 in which the presenting symptoms were from metastases. Björk[7] notes that many articles give the percentage of various symptoms present at the time of the final diagnosis, but this is usually late in the disease. Furthermore, cough, chest pain and hemoptysis, often listed as the most common symptoms in primary cancer of the lung, are not pathognomonic of cancer but occur in pulmonary tuberculosis, bronchiectasis and other chronic pulmonary diseases. Ochsner, DeBakey and Dixon[17] and Overholt and Atwell[18] have also emphasized the lack of a characteristic clinical picture in primary malignancy of the lung.

From the foregoing, the significant implication is that there are often no symptoms early in this condition. The logical corollary to this is that if cancer of the lung is to be detected when a cure is possible by surgery, it must be found before there are symptoms. This was

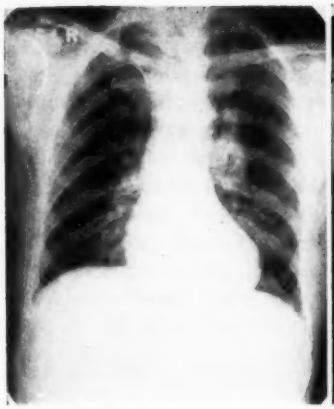

FIGURE 6. Case 6.

FIGURE 7a

FIGURE 7b

Case 7.

stated by Adler[1] in 1912 but has only begun to receive adequate attention in the last few years. Overholt and his co-workers[18-21] have devoted considerable study to this matter. Their conclusions may be summarized in the following statements:

1. Early, there are no symptoms in primary cancer; therefore, routine survey films are necessary for detection.

2. If detected during this "silent" phase, the likelihood of extrapulmonary extension is low and cure rate should be high.

3. When symptoms are present, the chances of extrapulmonary extension are high and the cure rate is low.

4. The longer surgery is delayed, the lower the resectability rate (and the cure rate); hence, exploration should not be delayed if all other diagnostic measures fail.

Overholt[20] cites a citywide survey made in Boston in 1949 in which 536,012 satisfactory films were obtained. Of these, 398 were considered possible tumors; 333 were followed up and 76 found to be cancer, type not stated. (Later, 43 of these were found to be primary lung cancer, or 8 per 100,000.) Overholt[20] also mentions a United States Public Health survey of 1,095,569 persons in 3 cities using 14 x 17 films. In this group, 0.1 per 1000 were found with primary pulmonary malignancies of all types. The true survey figures for cancer should actually be higher since some cases are undoubtedly followed as tuberculosis (emphasized by Overholt[20]). Gowen and Frank[22] in a survey of 156,724 individuals using 70 mm. films found 14 proved cases of cancer of the lung, 10 primary. Since 9 of these persons were more than 50 years of age, they suggest surveys be conducted above the age of 45. However, of 1,751 patients in our series, there were 2 per cent from 35 to 40 years of age, 13 per cent from 41 to 45, and 17.5 per cent from 46 to 50. Since the machinery of making surveys for tuberculosis is already available, it would add little to the cost to include all persons over 40 (and preferably over 35) and this could be expected to add appreciably to the number of early cancers of the lung discovered.

Routine films of the chest in hospital patients should afford a more fruitful field for detection of cancer as well as of tuberculosis; this is already being done in a number of hospitals, and this practice will probably become more widespread when economic difficulties are overcome. At Hines Hospital, routine chest films have been done on all admissions for several years. (Many of our cases have been discovered by this means.)

An idea of the effectiveness of surveys in detecting cancer of the lung can be obtained by comparing the incidence found in Connecticut by MacDonald[23] with the figures given by Overholt.[20] The 7 year average for

primary malignancy of the lung from 1940 to 1946 in the state of Connecticut, with a population of 1,750,000, was 13.1 male and 2.7 female, or 7.9 per 100,000. For the year 1945, MacDonald[23] reports 19 male and 2.6 female, or 10.8 per 100,000. Thus, the 8 per 100,000 in the Boston survey and the 10 per 100,000 found by the United States Public Health study compare favorably with MacDonald's figures. (Unfortunately, both types of statistics for the same geographic regions are not available to us.)

Finally, it is rather enlightening to realize how little progress was made until quite recently in detecting early cancer of the lung since Adler's[1] monograph in 1912. There have been, of course, refinements in technic such as body section radiography, the improved bronchoscope and newer methods of cytology of the sputum. But the basic concepts were clearly laid down by Adler,[1] who stated that in order to find cancer of the lung when it could be successfully treated, it would be necessary to make routine x-ray examinations of all patients before they have symptoms; and further, that if a suspicious lesion were found and all examinations including bronchoscopy and sputum examinations were negative, exploratory thoracotomy should be resorted to just as exploratory laparotomy was already being used in abdominal cases. He also mentioned that Lenharz had already done a successful lobectomy for cancer of the lung. Adler[1] himself had for some time been routinely fluoroscoping all his patients and making films (plates) of the chest in suspicious cases, at a time when the available equipment was relatively crude. Perhaps the only real advance has been the survey method, and this has only begun to be used to any extent in the last 3 or 4 years. It is true that much had to be done to implement Adler's concept. First, the idea of the rarity of primary cancer of the lung had to be dispelled; for instance, at Hines Hospital, the incidence of primary carcinoma of the lung for over 10 years has been more than twice that of carcinoma of the stomach. Then the idea that the entire lung could not be removed successfully had to be overcome, and later, the prohibitive mortality of such a procedure had to be successfully combated. Newer technics of anesthesia and thoracic surgery and the advent of antibiotics, by greatly reducing the operative risk, have undoubtedly given impetus to a more aggressive attack on the problem of lung cancer.

It is to be hoped that when chest surveys become more widespread and follow-up of suspicious lesions becomes more effective, many more cases of primary cancer of the lung will be found when curative surgery is not only possible but also probable.

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Evaluation of Present-Day Treatment of Peptic Ulcer

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The diagnosis and treatment of uncomplicated duodenal ulcer is discussed, including both medical and surgical treatment. A medical regimen is preferred, if the patient's symptoms can be controlled and if there are no complications. A patient is presented and her case described.

To start the discussion of our concept of management of uncomplicated duodenal ulcer, I would like first to present a patient to you, then to cover the program we follow—which we believe is reasonably successful—and to mention a few items about complications.

H. MARVIN POLLARD

The patient present is here in response to my request to the Clinic Committee for a patient with a duodenal ulcer. I saw her for the first time about half an hour ago, and I believe you will agree that hers is a completely atypical case of duodenal ulcer. She is most cooperative and was good enough to come to us this morning in order that we may see her and talk over her history.

Shirley, will you first tell us how old you are?

PATIENT: I am 53 years old.

DR. POLLARD: In talking to her a few moments ago I discovered that her first digestive disturbance occurred about 24 years ago.

PATIENT: That's right.

DR. POLLARD: Interestingly enough, that was a vague upper abdominal discomfort. Subsequently a diagnosis of cholecystitis was reached and she had a cholecystectomy at that time. Her gallbladder and appendix were removed and a hernia was repaired. She experienced no further difficulty.

Incidentally, did you have any stones in your gallbladder at that time?

PATIENT: I don't know; I was so sick I don't know what they told my husband.

DR. POLLARD: At any rate, she had no recurrence of her digestive difficulties until about 4 years ago; at that time where did you start noticing discomfort?

PATIENT: I began to have a sharp pain on the left side. It felt just like a little marble or something like that.

DR. POLLARD: You could put your finger right on the location of that pain?

PATIENT: That's right.

DR. POLLARD: What time of day would that occur?

PATIENT: It always woke me at night around 1:30 or 2:00 o'clock. I thought it was gas.

DR. POLLARD: And what would you do to relieve it?

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PATIENT: After it began to bother me so much, I took the soda box to bed with me and would get up during the night and drink a little soda water and try to belch off the gas.

DR. POLLARD: Would that relieve you?

PATIENT: No, and the next time I would take ALKA-SELTZER®, and finally I would go to sleep.

DR. POLLARD: What were those "Big Sixes" you took?

PATIENT: I have trouble with my bowel movements and I have to take a physic, sometimes a dose of "Big Sixes," sometimes Epsom salts—not every day, but about twice a week.

DR. POLLARD: If you did that, would you get relief for this discomfort?

PATIENT: That's right.

DR. POLLARD: Were there periods of time, intervals of several weeks, when you did not have any discomfort at all?

PATIENT: I would go for a week, would feel fine and wouldn't have any pain; all at once, some morning, it would bother me and hit me some nights. I would have a sharp pain, feel sluggish, drooping, with no energy.

DR. POLLARD: Do you work?

PATIENT: No.

DR. POLLARD: How many children have you?

PATIENT: I never had children.

DR. POLLARD: You told me a while ago you had to get the children off to school.

PATIENT: Those ain't my children; they're the children I take care of at the house.

DR. POLLARD: You are married?

PATIENT: My husband is sick. He has a bad heart and high blood pressure and had a stroke.

DR. POLLARD: What happened to you a week ago Thursday?

PATIENT: A week ago Thursday I was in the bed, I just felt tired; I did a big laundry the night before, and thought I was tired from working at night. I felt sick to the stomach and dizzy. When I lay down I felt pretty good, but I felt dizzy when I tried to get up and I seemed to move backward. I told my husband, "I feel funny."

He said, "Go lay down." I said, "I'm not going to let it get the best of me." I tried to make breakfast but I fell back. I didn't go to bed, but just lay on the davenport in the front room. After a time, I went to the basement to take down my laundry. When I had taken down 2 or 3 pieces, I went backwards and just flopped down in a chair.

DR. POLLARD: How soon after that did you vomit?

PATIENT: While I was down in the basement I bumped a chair on the floor so my husband could hear me. He said, "What is it?"

I said, "I'm sick. Get me out of here." He couldn't lift me because he's sick.

He said, "What do you want?"

I said, "There's some medicine upstairs in the bedroom that the doctor left for me." He brought the medicine to the basement and gave me a dose. I said, "Just let me sit down here now; you go on back and leave me alone."

DR. POLLARD: Shirley, after a few minutes you vomited, didn't you?

PATIENT: I did.

DR. POLLARD: It was very dark?

PATIENT: After a while I went upstairs and I began to feel a phlegm boiling up in my throat. I said, "Go get me a pail," and as soon as I tried to get up again I vomited something.

DR. POLLARD: She told me a while ago that when she vomited she noticed it was a black material, and that while she was in the bathroom she likewise went to the stool. Whereas ordinarily she does not notice her stool, on this occasion she did, and it was just as black as it could be. Did it look like black tar?

PATIENT: Just like black tar you see out in the street.

DR. POLLARD: She called her physician shortly after that. He came, and he was the one who took you to the hospital, wasn't he?

PATIENT: I told him, "I can't go today, I have to wait." So I didn't come in until Monday. That was on a Thursday. There was no one to take care of my house and my sick husband.

DR. POLLARD: When did they take your x-ray?

PATIENT: I think it was last Friday.

DR. POLLARD: Tell me one more thing. How

much do you weigh at this time?

PATIENT: Well, when I went into the hospital last Monday I didn't weigh but 251½ pounds.

DR. POLLARD: You're really losing!

PATIENT: I think I lost quite a bit. They starved me out for 2 weeks. I didn't get food, water, milk; I didn't get nothing.

DR. POLLARD: When this patient was admitted to the hospital, her hemoglobin was 10.2 gm.; her red blood cell count was 4,200,000, and her white blood cell count was 6,950. Her treatment consisted essentially of aluminum hydroxide every hour and 600 cc. of milk every day.

Her x-rays show 2 things: (1) what the roentgenologist interpreted as a prolapse of the gastric mucosa, and (2) an active duodenal ulcer crater in the duodenal bulb. Both conditions could account for her bleeding, admitting that in all probability it is coming from the duodenal crater. The characteristic appearance of prolapse can readily be seen in the x-rays.

I am very glad to be able to show the patient because I think it is the unusual, atypical case that confuses us far more often than the typical. None of us has difficulty establishing a diagnosis in the case of an individual who is tall, slender, tense, nervous, unstrung, worried about business, worried about domestic problems, and so on. It is this other type—the unusual problem—that makes it more difficult for us, particularly where the case is complicated with prolapse of the gastric mucosa in addition to an active duodenal ulcer crater.

Going back just a little, I think the recent work on section of the vagus fibers for treatment indicates somewhat the association between worry and gastric function. Also, the whole concept of the adaptation syndrome emphasizes the constant association during stress of the formation of erosion, stasis, hyperemia, derangement in tissue nutrition, breakdown of cells, and, finally, exposure to highly destructive gastric juice. With the alarm reaction, there is acute gastric and duodenal hyperemia and erosion, sometimes with hemorrhage into the stomach, as a constant and characteristic manifestation of the first stage in the general adaptation syndrome. These factors merely indicate that the etiology, at least, may be associated with stress, although this is not always so.

In handling such patients, one of the major problems that concerns us is the prevention of recurrences. Any of us can usually stop the acute episode, but the prevention of recurrences is really the thing that we aim for. Usually we are faced with individuals whose ulcers are intractable, and, as Dr. Walter L. Palmer has pointed out, it is commonly the patient that is intractable rather than his ulcer. It is for this reason that it is so helpful to be able to sit down with these individuals, to find out what they do in a 24 hour period, to learn what the patient's 24 hour day includes. The patient here does not have children of her own; she is taking care of foster children; her husband is ill. With her, as well as with many of the rest of us, there are problems, I am sure, that concern her. If we can control the situation by placing the patients on a good diet, by getting them on a reasonably good daily program, by controlling their day-by-day activity with increased vacation periods and with rest and relaxation, then we can prevent recurrences.

Assuming that we are faced with a complicated situation, what is the first thing to do? We must be absolutely sure about the diagnosis, first of all. It is true that the x-ray is highly efficient in most instances. I don't think any roentgenologist can tell us exactly how efficient an x-ray is; no one knows how many negative upper gastrointestinal series actually occur in patients with active duodenal ulcers. Therefore, I want to emphasize that when you have a good duodenal ulcer history—even though the roentgenologist may report a negative upper gastrointestinal series—treat that patient for a duodenal ulcer and do not be misled by the roentgenologist's telling you that the upper gastrointestinal series is completely negative.

My good friend Dr. David J. Sandweiss in Detroit recently surveyed a group of 19 patients with posterior penetrating duodenal ulcers. He followed those individuals all through

their stories up to the time of their operations. For years, all 19 patients had been treated by various doctors as having psychoneuroses with functional gastrointestinal disturbances. Why? Because in almost every instance the roentgenologist had not been able to identify the posterior penetrating duodenal ulcer and, hence, the physician was misled into treating the patient as a psychoneurotic rather than as an individual having an active duodenal ulcer. It is true that the ones he followed all came to operation, so that he was able, subsequently, to prove the diagnoses of posterior penetrating duodenal ulcers.

In patients with gastric ulcers it is of value first to demonstrate roentgenographically the absence of malignancy and, second, to know when the lesion is healed. To illustrate: In the case of a 36 year old woman with typical benign gastric ulcer, there was a large, deep crater with a glistening white base by gastroscopy, a smooth, rounded overhanging edge and with no evidence of nodularity in the surrounding mucosa. I followed her at monthly intervals with upper gastrointestinal roentgenographic series as well as by gastroscopy. She was completely edentulous and did not seem to object to the monthly gastroscopic examinations. At the end of 6 months she still had a small active ulcer crater. Believing that I had gone far longer than I should have in allowing a benign gastric ulcer to heal, a subtotal resection was performed and a benign ulcer was found. I do not recommend 6 months as the time to follow these individuals; I merely point out that we did delay in this instance and the lesion was benign.

In contrast is the case of a young man, 26 years old, who had been seen in our clinic on 3 different occasions. First it was thought that he had a functional disturbance. On the third visit his physician ordered an upper gastrointestinal x-ray series which showed a definite filling defect, surrounded by heavy nodularity, in the lesser curvature of the stomach—entirely typical of an ulcerating gastric carcinoma. By gastroscopy he likewise showed the characteristic features of an ulcerating gastric carcinoma consisting of the filling defect in the midportion of the gastric ulcer, extensive nodularity in the prepyloric area, and complete absence of peristalsis in that entire area. The other feature consisted of blending of the surrounding mucosa with the ulcer crater. When those features are found one can be reasonably sure that one is dealing with a malignant rather than a benign process. Interestingly enough, this patient's gastric analysis showed free acid reaching to 110 degrees.

I believe that the gastric analysis is highly valuable in making the differentiation. If there is achlorhydria you can be almost sure that you are dealing with a malignant process and not a benign ulcer. It is important to be sure, however, that the tube is in the stomach and not curled up in the esophagus before you can be certain about the presence or absence of achlorhydria.

Treatment

Going from the diagnosis to the treatment, I honestly believe that bed rest is highly important. I concede that where you are faced with patients working in industrial plants—individuals on the assembly line, individuals who must meet their payrolls, who must meet their day-by-day responsibilities—it is extremely difficult to persuade such patients to take time off and go to bed. However, one of my early errors occurred with a lawyer who had a duodenal ulcer. He convinced me that he did not need to go to bed to cure his ulcer. I was convinced, and placed him on all of the ulcer program with the exception of bed rest. A few months later I was seeing patients on rounds with Dr. R. C. Brown in Chicago and the very first patient we saw was my lawyer patient who was then in bed in the hospital with a recurrence of his ulcer. Dr. Brown merely indicated to me that the only thing he had done differently was to put that patient to bed. I don't think you can put them all to bed, but it still is a highly important factor in the recovery of these individuals.

The second important factor is the diet. We all have our pet diets. It was my privilege, a few years ago, to entertain Dr. Meulengracht from Copenhagen for a period of time, and I informed him that we were using his diet in the management of duodenal ulcer.

He told me that he had no specific diet, that all he wanted these individuals to do was to eat. If they would eat 6 times a day, he didn't really care what items they chose to eat at any particular meal.

I must admit that what we classify as the Meulengracht diet consists principally of ground meat, custards, eggs and milk, with 6 feedings per day; I believe that multiple feeding is the important thing. The diet should be high in protein since protein is very efficient in absorbing hydrochloric acid.

The next item is the alkali; I still believe that some alkali is of distinct value. I think it should be given at a time that will not inconvenience the patient. I am not in favor of the hourly administration of alkali because I think it is too often and not necessary, but if some good alkali is given 6 times a day, that is sufficient. I really don't care which alkali it is—aluminum hydroxide, magnesium trisilicate, calcium carbonate—all are highly effective.

I am still a strong believer in antispasmodics, such as belladonna, and particularly the atropine preparations which experiments have shown do lessen stomach motility. I believe that diminishing the motility is highly valuable.

Administration of atropine also effects a great diminution in the volume of secretion in patients with duodenal ulcers. By diminishing the motility and secretion with some well-accepted antispasmodic or antisecretory drug, I think we accomplish a great deal toward healing the ulcers.

BANTHINE® is undoubtedly a highly effective pharmacologic agent. There are a few contraindications to Banthine. One occurs when there is pyloric obstruction; the other, when there is prostatic disease. Another factor is the variability of the action of Banthine in some people. Now and then a patient may have considerable dilatation of the stomach associated with the administration of Banthine. In my estimation, one of the major criticisms of Banthine is the fact that it was originally considered as the sole treatment for duodenal ulcer. Any time you want to use anticholinergic drugs, be sure that you also use other forms of therapy—a good diet, some alkali, sedatives and rest.

Another form of treatment, again proposed by Dr. Palmer and Dr. Kirsner at the University of Chicago, is the administration of deep x-ray therapy over the acid-bearing portion of the stomach. There is no question about the fact that these physicians are convinced that it is worth while; there is no question that it will diminish both secretion and acidity in the stomach for a long period of time, and the figures are quite convincing that it will prevent recurrences in a large number of individuals. I have limited its use to patients with extensive degrees of hypertrophic gastritis particularly associated with a duodenal ulcer. I have not used it in a large group of cases as yet. I still think it has something to offer patients with intractable duodenal ulcers.

We recently had an ulcer patient from Ann Arbor for whom I used x-ray therapy because he had no obstruction, and there was no evidence of any complication, but he was having a lot of difficulty and he had been in the hospital 3 times in one year. We eventually gave him x-ray therapy over his stomach. Unfortunately the experiment was not well controlled for the simple reason that his political opponent was elected just about the time I finished his x-ray therapy, and I don't know which factor is going to be more efficacious in his case.

I doubt very much that either KUTROL® or enterogastrone has any particular beneficial effect in preventing recurrence of duodenal ulcer. There is no question that these drugs have a pharmacologic action in dogs, but I have not had much success in the administration of either of these products in humans.

Cleveland is the home of the drip method for the treatment of duodenal ulcer. I must admit that if I can give most of my patients a little AMPHOJEL® or milk at the bedside, they can take it just about as well as though I put a tube down into their stomachs and left it down. In England recently, however, I found that they were treating many of their duodenal ulcer patients by the drip method. I have not used it much, since I do not believe it is necessary, although I admit that it is effective.

I do think it is valuable to restrict the use

of tobacco in these individuals. Actually you will have to evaluate your patient in that regard. There are doctors, who have seen many more cases of duodenal ulcer than I, who believe that the use of tobacco must be stopped completely and permanently. The same is true of alcohol. In general, I have not been that rigid, but I do think it is desirable to limit it.

I would like to mention 2 contraindications of which we must be aware in following patients with duodenal or gastric ulcers. One is the utilization of a splanchnicectomy in a person with a duodenal ulcer. Once you cut the splanchnic nerves you eliminate the pain fibers in these people, and forever after they will be unaware of perforations or of the symptoms of recurrences in case they develop them. We have discontinued the practice of doing a splanchnicectomy on patients with high blood pressure and duodenal ulcers.

The other contraindication is the utilization of ACTH and cortisone in individuals with duodenal ulcers. I feel very strongly that neither ACTH nor cortisone should be used in patients who have duodenal ulcers. If we carry these patients along with good diets, with rest, with a change in their daily programs, with alkalis and antispasmodics, I believe that the majority certainly can be controlled.

What happens when complications occur? I will tread in that territory rather lightly, but we have had the opportunity of following 2 groups of patients in our hospital, both operated on by the same general group of surgeons, following similar surgical technics. Of one group of 70 patients with vagotomy and gastroenterostomy, 36 patients were followed for 5 years. The second group, having the same indications for operation, underwent subtotal gastrectomies.

The 5 year results on 18 patients, followed for 5 years, showed that vagotomy with gastroenterostomy was satisfactory for 85 per cent and that subtotal resection was satisfactory for 86 per cent. So far as end results are concerned, keeping in mind the recurrence rate, hemorrhage and perforation, the 5 year results in those 2 groups were similar.

However, if you evaluate such other factors as operative mortality, it was found that the operative mortality for the group which had subtotal gastrectomies was 5.6 per cent: the operative mortality in our group of 70 patients who had vagotomies with gastroenterostomies was zero. That, to me, is a significant differentiation.

The postoperative nutritional manifestations were significantly different in the 2 groups.

As a result, at present we are doing more vagotomies with gastroenterostomies than subtotal gastrectomy procedures. Nevertheless, I think both operations still have their followers and there are particular situations for both operations. In general, we should treat most patients who have no complications with a medical regimen and, if we can, spend time with them, learn what they are doing, get them to take a few more vacations, teach them a little more self-assurance since these people have no self-assurance whatsoever. By giving them a little confidence in themselves, a little confidence in their jobs, a little better understanding of their domestic situations and their problems, I think we can control their symptoms effectively.

Management of Serious Scalp Injuries

MORRISON D. BEERS* AND FRANK W. PIRRUCCELLO**

Chicago, Illinois

Two cases of serious scalp injury are reported, and methods of treatment are discussed. The early covering of denuded bone and pericranium with full-thickness scalp rotation flaps and/or split-skin grafts as indicated will result in success in these often serious injuries, and the rehabilitation of the patient will be prompt.

SCALP injuries, especially those complicated by the loss of tissue, invariably are serious surgical emergencies. Two factors of paramount importance in their management are (1) control of infection and (2) restoration of an acceptable cosmetic appearance. Numerous articles have appeared in the literature during the past decade on the management of complete or subtotal scalp avulsions,[1-5] but it was felt that a review of scalp injuries of lesser extent might be of value.

FIGURE 1. Convertible top crushed when car overturned after tire blew out. Girls were in rear seat of car.

M. D. BEERS

The 2 patients to be described were 16 year old girls who sustained scalp injuries when the convertible automobile in which they were riding blew a tire and "turned turtle." The canvas top was crushed in and torn (Figure 1), and the girls' heads were scraped along the cement-paved road. After emergency treatment at the scene of accident by the Michigan state police, the girls were sent by ambulance to the Mt. Carmel Hospital Emergency Room, Detroit, Michigan, where they arrived at 3:00 A.M.

Case Reports

Case 1—On admission to the hospital, this

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16 year old girl had a scalp loss 8.5 by 7.5 cm. involving the left temple and forehead area, and a partial avulsion of the helix of the left ear and lower portion of the concha and lobule (Figure 2); in addition, there was an abrasion of the left cheek. The patient had not been unconscious at any time, and radiographs of the skull revealed no evidence of fracture.

The past history and physical examination of the patient were not significant except for the injuries already described, and a grade 1 rheumatic valvular heart disease of four years' duration.

The preoperative condition of the patient was well stabilized, and preoperative preparation consisted of the administration of combined tetanus and gas gangrene antitoxin, S-R penicillin and light sedation.

Seven hours after the injury, the patient was taken to the operating room. Anesthetic was administered, consisting of combined intravenous PENTOTHAL®-curare and endotracheal nitrous oxide-oxygen mixture. The hair was removed from most of the scalp with an electric clipper. The entire scalp and avulsed area were prepared with a *p*HISODERM® solution, the wound was irrigated copiously with saline solution and all road dirt and foreign particles were removed. The abrasion on the cheek was scrubbed vigorously with a hand brush to remove imbedded road dirt. The pericranium had been partially abraded, and there were grooves in the outer table of the cranium; the diploic space, however, had not been penetrated. The scalp area was again scrubbed and irrigated, jagged wound margins were debrided and several long shredded flaps from the posterior margin of the wound removed. A Gillies rotation flap was advanced from the left parietal region into the defect (Figure 3). A Z-plasty was then carried out in the lower left temple area to relieve tension in this portion of the flap. NYLON® zytor interrupted sutures, size 2-0, were used throughout in the repair of the flap. A skin graft of moderate thickness was then sutured into the defect resulting from the Gillies rotation flap. The graft was placed over the intact pericranium, where it was held in position by a

FIGURE 2 *(Case 1)*. Preoperative photograph showing area of scalp loss, area of denuded cranium, cheek abrasion and partial ear avulsion.

FIGURE 3 *(Case 1)*. Immediate postoperative photograph showing closure of scalp defect by use of a Gillies rotation flap from the vertex. Note tie-on pressure onlay dressing retaining the skin graft in place.

FIGURE 4 *(Case 1)*. Immediate postoperative lateral view showing Z-plasty of left temple area at hairline and definitive repair of helix.

FIGURE 5 *(Case 1)*. Healed skin graft two weeks postoperatively.

FIGURE 6 *(Case 1)*. Posterior view of skin graft showing excellent take on pericranium.

FIGURE 7 *(Case 1)*. Definitive result at eight months. The protruding ears, which had existed prior to the accident, have been corrected.

tie-on onlay pressure dressing (Figures 3 and 4). The exposed ragged ear cartilage was then removed, and the avulsed helix was covered with advanced preauricular skin. The lacerations of the ear were sutured with 6-0 braided silk. A VASELINE® pressure dressing was then put over the entire scalp, left cheek and ear.

The patient was given 1500 cc. of whole blood during the operation, and her condition remained good. Her postoperative convalescence was uneventful. Figures 5 and 6 show the healed scalp and skin graft two weeks postoperatively.

The skin graft was subsequently removed in three stages by multiple excision, to provide complete continuity of hair-bearing scalp. A bilateral ear-plasty was ultimately performed to correct the patient's type 3 protruding ears, which of course existed at the time of the accident. Figures 7 and 8 show recovery of the patient eight months after her scalp injuries had been sustained.

FIGURE 8 *(Case 1)*. After removal of skin graft by multiple excision, to provide complete continuity of hair-bearing scalp.

FIGURE 9 *(Case 2)*. Preoperative photograph showing jagged scalp laceration and accompanying tissue loss.

Case 2—This 16 year old girl was admitted to the Mt. Carmel Hospital at the same time as the patient in Case 1. Her condition on admission was good except for the profuse bleeding from a scalp laceration which extended from the forehead in the midline toward the vertex (Figure 9). A large traumatic flap was also partially avulsed on the left side of the wound. The patient had not been unconscious at any time, and radiographs of the skull failed to reveal any evidence of fracture.

Five hours after the injury, the patient was taken to the operating room, where the hair was clipped and a *p*Hisoderm preparation of the face and scalp was carried out. Sterile drapes were placed about the head. Infiltration anesthesia (1 per cent NOVOCAIN®) was used to produce nerve block. The wound in the subaponeurotic space underneath the traumatic flap was found to contain impacted road dirt and gravel. The pericranium was entirely avulsed in the area of the flap and there were grooves in the bone (Figure 10). This area was scrubbed vigorously with a hand brush, foreign material was removed, the contused wound margins were debrided and the area was irrigated with saline solution. The wound margins were generously undermined, the wound thus being converted into a linear type of wound. The hair-bearing scalp areas were closed with 2-0 zytor nylon interrupted sutures. The forehead areas were closed with 2-0 zytor nylon continuous subcuticular sutures. The subaponeurotic space was drained with two Penrose drains for a period of 48 hours. A pressure dressing was placed over the wound and tied in place with three previously placed tension sutures. An ACE® fluff pressure dressing was applied over the entire scalp and forehead.

Postoperatively the patient did extremely well, and she was allowed to go home on the third postoperative day. The healing scalp, two weeks following the operation, is shown in Figure 11.

Discussion

Patients with scalp injuries constitute surgical emergencies and must be carefully observed to properly evaluate cerebral and cranial damage. The accepted rules for the management of soft-tissue injuries apply also to the scalp. Contrary to a somewhat prevalent attitude that scalp injuries will always heal without infection, serious infection can and does occur. Dr. Harry Mock[6] decries the careless attitude existing in most emergency rooms in regard to scalp injuries. Although posttraumatic infection may occur but rarely, the consequences of intracranial abscess and its complications must be borne in mind. Therefore, the most meticulous application of good surgical technic must be rigidly adhered to at all times.

The vascularity of the scalp is unique. The very copious blood supply promotes rapid healing, and infection is relatively rare in

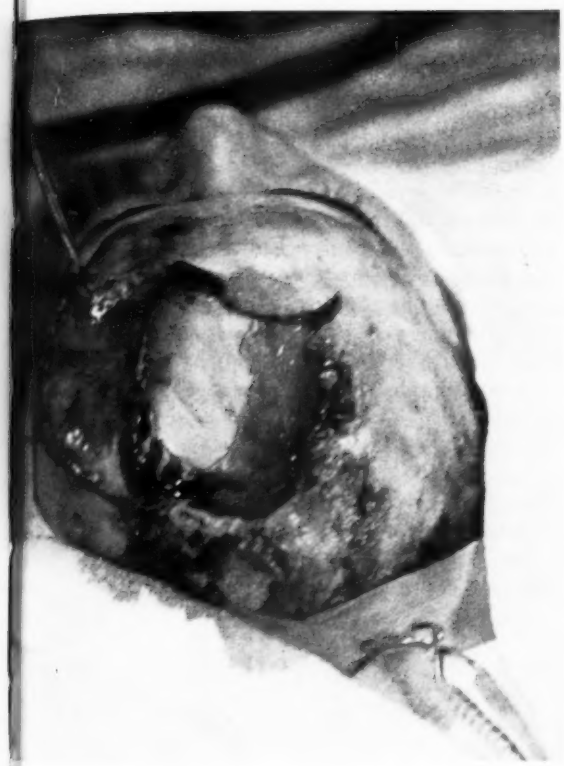


FIGURE 10 *(Case 2).* Preoperative photograph showing large traumatic scalp flap with underlying area of pericranial loss. This patient required only one operative procedure.

most scalp wounds. This rich blood supply also makes possible the shifting of large pedicles and rotation flaps with practically invariable success.

The principles to be observed in closing of scalp wounds are (1) wound closure with a minimum of tension; (2) covering of cranial defects with full-thickness scalp without the suture line overlying the defect, and (3) immediate covering of denuded bone and/or pericranium. The management of cranial and cerebral defects is, of course, best handled by the neurosurgeon. However, the principles of scalp closure remain the same.

The basic aims in closing scalp defects in accordance with the foregoing principles are fourfold: (1) scalp advancement, (2) relaxing incisions, (3) rotation flaps and (4) application of free skin grafts.

When there has been little or no tissue loss, the majority of scalp lacerations can be closed by debriding the margins of the wound and suturing them together, without undermining the scalp. Debridement is conservative, and the removal of ragged and contused tissue will insure less scar tissue formation. When tissue loss is minimal, the wound is extended in both directions with S-curved incisions to distribute tension over a greater area, thereby reducing tension in the immediate wound area. Scalp tissue, unlike skin, does not advance readily because of its firmness and relative inelasticity. Extensive undermining is necessary to advance scalp tissue in any appreciable degree. The ratio may be 6 to 9 cm. of undermining in the subaponeurotic space for each 1 cm. of scalp tissue to be advanced.[7] Multiple parallel incisions from the underside of the scalp can be used as an adjunct in stretching the scalp. These incisions are carried through the aponeurosis and

FIGURE 11 *(Case 2).* The healing scalp, two weeks postoperatively.

subcutaneous layers, but not through the skin itself. The tripartite technic of Cushing is a type of scalp shifting and advancement. The wound edges are debrided and excised so as to produce a triangular defect. The angles are then extended therefrom in a long curve. The one disadvantage of this type of closure is that the suture line may overlie the area of fracture site; thus, in some types of cranial wounds other procedures of scalp shifting are preferable to place the suture line away from the area of cranial injury.

Relaxing incisions are made parallel to the line of closure of the initial wound. These may be single or multiple, but must be longer than the initial wound to be efficient in reducing tension and to expedite the repositioning of scalp tissue. Relaxing incisions produce, in effect, bipedicled flaps. They are especially useful in forehead defects, where a fine line closure is desired. An extremely satisfactory cosmetic result can be achieved through the use of local tissue of full skin thickness. The secondary defect is then split-skin grafted within the hair-bearing area. The skin graft can subsequently be excised multiply, if so desired.

The sliding rotation flap, as advocated by Sir Harold Gillies,[8] is exceedingly useful in scalp wounds, especially when these are associated with an underlying cranial defect. Tension on resuture is distributed over a wide area and removed from "the point of danger." Such a rotation flap is cut by incising in a wide curve, so as to produce a hemisphere flap. The end of the incision can also be "dog-tailed" (this was the technic used in Case 1). A diagram for cutting such a flap is shown in Figure 12. Variations in its use are shown in Figure 13.

Small and Turner[9] of the Royal Army Medical Corps report an extensive experience

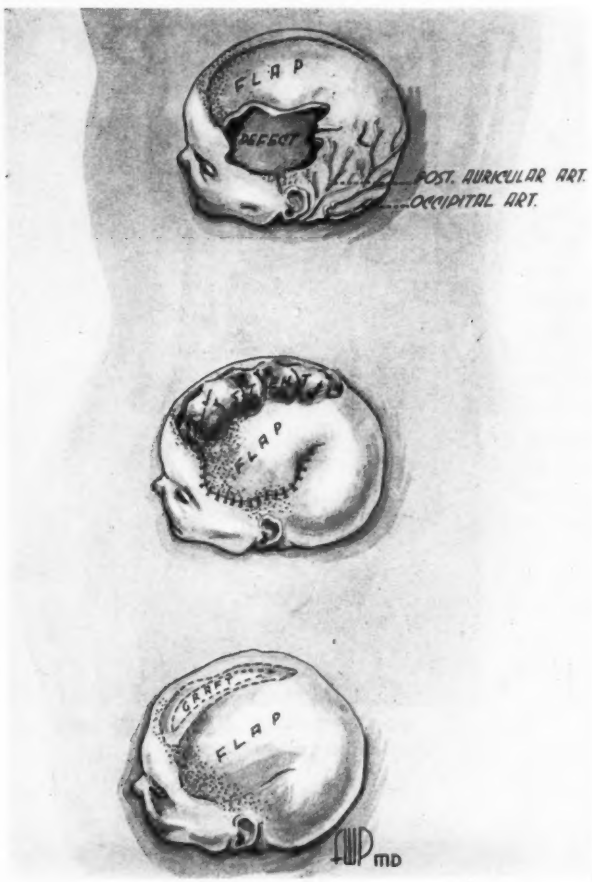


FIGURE 12 *(left)*. Diagrammatic recapitulation of Gillies' rotation flap technic. A tie-on pressure stent will assure a complete take of the split graft on the pericranium.

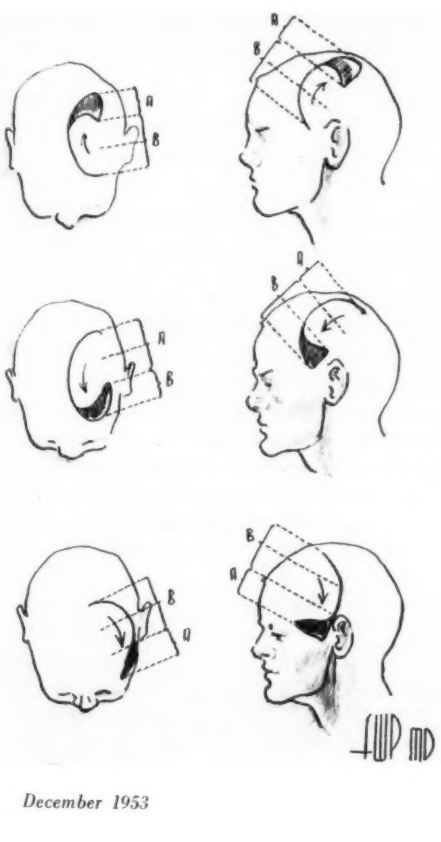
FIGURE 13 *(right)*. Versatility of the Gillies rotation flap diagrammatically illustrated. The size of a rotation flap is patterned by projecting the width of the defect at least two times beyond its margin. Incision is accomplished in a wide arc, extending from the far side of the defect to the projected point. Thus, B is two times A. Such flaps must be generously patterned to relieve and distribute tension adequately.

with war wounds of the head in some 1200 cases from the E.T.O. They state: "Scalp defects were never closed by direct advancement, but by a variety of flap methods. The great majority of defects, even of large size, could be closed by the sliding flap method. . . . The true rotation flap is used principally with large basal area defects in the frontal region. A portion of scalp containing a vascular pedicle is rotated to the excised wound area and the donor site covered with a Thiersch graft." The rotation flaps were usually done by Major FitzGibbon of the Maxillo-Facial Surgical Unit.

The methods of shifting scalp already described are useful in covering bare bone. If bone is not covered, it will die. Bare bone cannot be covered successfully with split-skin grafts. However, when the outer table of cranial bone is thinned and perforated in multiple areas by the use of a chisel, a split-skin graft can be applied with a reasonable assurance of taking. A procedure used in early American pioneer days was that of drilling multiple holes through the outer plate into the diploic space. An awl was used to produce the holes. Granulation tissue would then grow from the holes and spread across the surface to produce a closed wound. The "know-how" of drill holes in scalping injuries of the American frontier days is excellently presented in an article by Strayer.[10]

The pericranium must be covered promptly or it will gradually disappear.[11] Split-skin grafts can be applied to the pericranium with every reasonable assurance of a take. There are instances in which a split graft is most appropriate in repairing scalp defects due to trauma, or those following the excision of malignant lesions. The local area can then be observed for a possible recurrence of the neoplasm. Split grafts on the head remain smooth, become pliable, and thicken, and the edges level off at the suture line so that often a definitive result is obtained which is quite acceptable to the patient.

Failures with the use of pedicle flaps of the scalp are due primarily to disturbances in vascularity. Such disturbances may be the result of (1) pedicle flaps with the base at the midline or in the basal area in which a main vascular channel may have been interrupted, (2) infection, with resulting thrombosis of the vessels and (3) inept or excessively tight pressure dressings.



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DIAGNOSTIC CLINIC

Postphlebitic and Varicose Vein Stasis

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The mechanism whereby progressive damage is produced by varicose and postphlebitic venous stasis is outlined. Incompetence of the valves in the perforating veins is of paramount importance in determining treatment. Venous stasis associated with gross incompetence of the perforators is not permanently relieved by any of the usual methods of treatment, but is controlled by applying a regulated air pressure to the lower leg. Cases are presented illustrating the effectiveness of this method of treatment.

W. J. MERLE SCOTT

THE extremely common problem of venous stasis in the lower extremities as expressed in varicose veins and postphlebitic lymphedema is due solely to the fact that man stands and walks on his hind legs. In the erect position the return of blood from a dependent area is opposed by the gravitational force of the column of blood from that level to the heart. For the average human adult this force is equal to approximately 75 mm. of mercury for the lower third of the lower leg. Thus you can see that this is a very significant fraction of the whole arterial pressure that must push the blood from the heart through the capillaries and back again to the heart. Without going further into an analysis of the complicated hydrodynamic factors it is obvious that such a gravitational force offers a serious obstacle to venous return and would produce a severe degree of venous stasis unless accessory factors intervened.

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Nature has provided such accessory factors. Time does not permit a discussion of all of them, but I do want to mention the two most important ones that are useful in preventing such an orthostatic venous stasis.

Figure 1 is a schematic drawing of the subcutaneous veins, and I want to call your attention to the greater saphenous and the lesser saphenous veins, and to the interruptions in the veins, which are valves. Note also the apparently short veins coming down and ending blindly at small circles. These are schematic representations of the so-called perforating veins which join the superficial and deep venous systems.

The main trunk subcutaneous veins, the greater and lesser saphenous veins, are provided, then, with a number of valves, all of which are so arranged that they allow only the flow of blood toward the heart. They break the continuous column of blood and carry the

weight of the column above them. They are the holding part of the mechanism—they prevent this hydrostatic pressure from going back and being exerted against the peripheral veins and capillaries.

The motor part of the mechanism can be called the peripheral venous pump. Figure 2 is a representation modified from a drawing in Homan's textbook which I think illustrates very well the relative size of the deep veins. The deep veins are shown in comparison with the superficial veins. You will note that the deep veins contain a large volume of blood, and you see at the arrows the so-called perforators that are shown schematically in Figure 1. The deep veins are under the deep fascia in the muscular compartment. When the calf muscles contract, these deep veins are compressed and this large mass of blood is pushed out and propelled powerfully upward toward the heart. At the moment of relaxation this large venous reservoir is empty and at a low pressure, so that blood is pushed into it from all surrounding areas. There are numerous small veins uniting this system of large deep veins with the subcutaneous veins. Since these intercommunicating veins perforate the deep fascia, we call them perforators; there are more than 250 of them below the knee and several in the thigh.

Each of the perforators also has a valve so directed that it allows blood to pass only from the subcutaneous to the deep veins. Therefore, blood is sucked into these voluminous deep veins at the moment of relaxation, and the valves in the perforators prevent blood from passing out from the deep veins into the subcutaneous veins. With the alternate contraction and relaxation of the calf muscle in walking, the blood is pumped upward against gravity toward the heart, not only from the deep veins but also by way of the perforators from the subcutaneous veins.

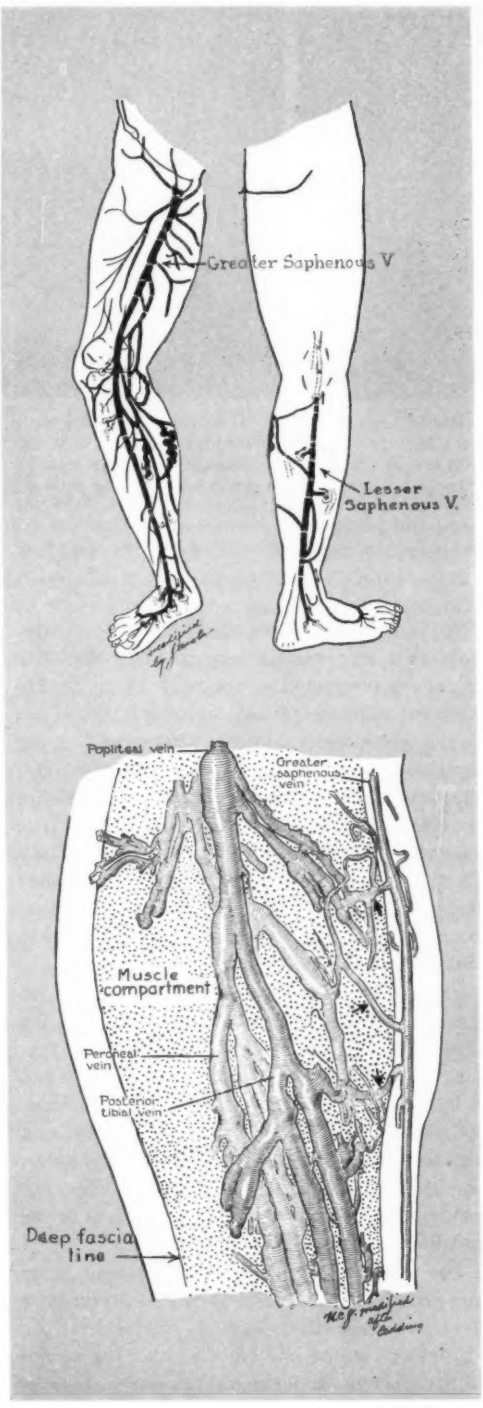

FIGURE 1 *(above)*. Schematic drawing of the subcutaneous veins, showing the greater and lesser saphenous veins, the valves and the so-called perforating veins which join the superficial and deep venous systems.

FIGURE 2 *(below)*. Relative size of the deep veins compared with the superficial veins.

FIGURE 3. Extensive large varicosities of the left greater saphenous system. On the left, the veins are tremendously distended in the erect position, and on the right the distended veins are emptied by elevating the leg. Rapid filling is prevented merely by pressure over the great saphenous vein just below its junction with the femoral, proving that the incompetence of valves is limited to the main stem veins and that valves of the perforators are competent.

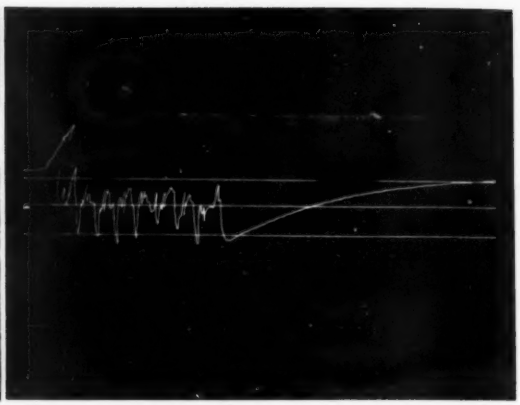

FIGURE 4. Normal venous system. Graphic representation of calf volume changes measured as pressure changes in an air plethysmograph surrounding the lower leg in walking. This shows the cyclic increase and decrease with each muscular contraction and relaxation with a decrease in total volume of the lower leg during the first few steps due to the propulsion of blood upward out of the veins in the lower leg. At the end of walking there is a very slow return in the mean volume due to gradual filling of veins through the capillaries.

A point I want particularly to make is this: Note that this mechanism requires that the valves be competent—not only those in the main subcutaneous trunk veins, but also those in the perforators. These valves in the saphenous veins are delicate structures and often eventually break down under the strain of constantly supporting the weight of the column of blood above them and also of taking the thrust of sudden increased pressure such as occurs with coughing, straining, and so on. The holding part of the mechanism has broken down when these valves give way.

Figure 3 illustrates a condition that I am sure all of you have seen many times. We have here very marked varicosities. The patient is put down on a table, his leg is lifted in the air, the blood rapidly leaves the large varicose veins under the effect of gravity, and with the hand held over the greater saphenous near its emergence from the femoral, the varicosities are completely empty and remain so for about 30 or 40 seconds.

The veins of the extremity become large and prominent, and this is the common type of varicose vein that develops during life; the perforators are competent and only the valves in main stem superficial veins (saphenous system) have broken down. This fortunately is easily restored artificially. By dividing the upper part of the saphenous vein above all branches under these circumstances, the varicosities do not fill by reflux flow and the venous stasis is prevented.

The Trendelenburg test in its simplest form is performed by placing a band around the extremity above the knee and one just below the knee; the tourniquets are lightly placed so that they prevent the movement of blood in the subcutaneous veins but not in the deep veins. After emptying the veins, with the leg depressed the veins remain emptied below that point when the perforators are competent; they fill rapidly, within 2 or 3 seconds, when the perforators are incompetent.

Unfortunately the valves in the perforators may also become incompetent. This is a much more serious condition, because, when their valves no longer function, the pumping action of the muscles is no longer effective in emptying the subcutaneous veins. It merely produces a to-and-fro motion of the contents, sucking blood through the perforators at the moment of relaxation but filling the subcuta-

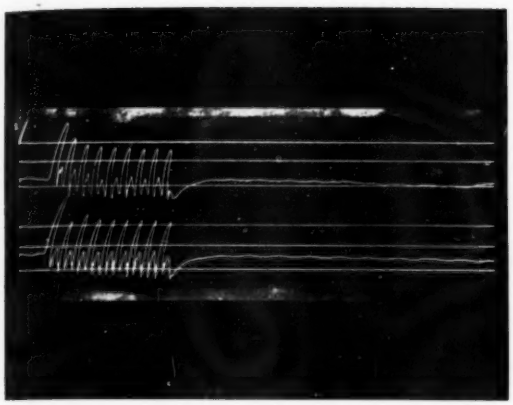

FIGURE 5. Venous system with incompetent perforators. This is the same type of graphic determination of calf volume as in Figure 4 in a postphlebitic extremity with gross incompetence of perforators, to be compared with the normal venous system shown in Figure 4. Note particularly the very rapid return to the original volume (within 3 to 4 seconds) on the cessation of walking. This is due to the fact that the veins fill retrogradely due to the absence of competent valves rather than through the capillaries as in the normal circulation.

neous veins during contraction. Also, these incompetent perforators transmit the gravitational pressure directly to the superficial veins.

In Figure 4 you see a graph showing the calf volume as measured plethysmographically in air during walking. With muscular contraction and relaxation there is a cyclic increase and decrease, but the mean volume decreases during the first few steps and then goes up and down cyclically. Note at the end of walking there is a very slow return in the mean volume; that is the normal venous return.

Note the difference in a case of incompetent perforators (Figure 5). The form of the curve is the same; the pressure relationships have made a little difference in the up-and-down movement, but that is insignificant. Again, for a couple of steps there is a decrease. Note, however, that the decrease in mean volume is much smaller than in the normal, and at the end of that time there is a rapid return. Actually this whole chart represents 60 seconds, so this return represents only about 3 to 4 seconds; in other words, the entire volume of the leg is recovered in 3 to 4 seconds, whereas it takes 30 or 40 seconds for such recovery in a normal person. The difference in volume is the amount of blood that the muscle propels out of it, and this blood drops back almost immediately—as soon as the muscular contraction is over—when the valves are incompetent.

When varicosities are of long standing, the perforators frequently have become incompetent. The familial type sometimes is seen, due to congenitally absent or deficient valves; the acquired type is more common. The varicose veins develop due to the repeated thrust on coughing, straining, and so on, as a result of which the delicate valves break down and typical varicosities appear.

The postphlebitic extremity with the typical swelling also is due to venous stasis; even if you cannot see or feel the veins, you can take it for granted that the perforators (not necessarily the valves in the main stem veins, but the valves in the perforators) have become grossly incompetent.

Uncontrolled venous stasis causes a progressive series of events: loss of an excess amount of fluid through the capillary walls, often accompanied by diapedesis of some red blood cells; accumulation of extracellular fluid, which slows the exchange of oxygen and metabolites and interferes with the nutrition of the cells; stimulation of the production of fibroblasts by the stagnant, protein-rich fluid, which also is an ideal culture medium for the growth of bacteria that may get in through the skin.

By these effects of venous stasis you can reconstruct the common complications seen in the postphlebitic patient (Table 1), and

TABLE 1

POSTPHLEBITIC COMPLICATIONS

Edema—lymphedema
Induration—chronic cellulitis—fibrosis
Venous stasis—varices with incompetent perforators
Pigmentation—preulceration
Stasis dermatitis and eczema
Attacks of recurrent cellulitis
Attacks of recurrent phlebitis
Ulceration

these are seen in long-standing cases of varicose veins also.

The first effect usually is edema, which we call lymphedema. Then there is a beginning induration of the tissues, a chronic cellulitis with fibrosis. There is venous stasis. Varices are apt to develop; though often you cannot see the veins and sometimes cannot feel them, you can be sure the perforators are incompetent. Pigmentation occurs, then pre-ulceration, then stasis dermatitis and eczema, attacks of recurrent cellulitis, recurrent phlebitis, and finally ulceration.

A typical postphlebitic state is shown in Figure 6. Unfortunately the induration cannot be felt, but the whole area is boardlike, purplish in the dependent position, and practically ready to break down. This is pre-ulceration.

Figure 7 shows the typical stasis dermatitis, with marked inflammatory reaction, oozing, cracking, and so on. These are the complications that occur as a result of the changes that venous stasis produces. If the venous stasis is not corrected or counteracted, these changes are apt to be progressive and ultimately the effect may be irreversible.

When there is gross incompetence of perforators, division of the saphenous veins alone will not materially influence the degree of venous stasis. Even stripping out the vein, which will temporarily interrupt the incompetent perforators, usually does not result in permanent improvement, because the perforating veins reunite with the superficial veins and the original condition recurs.

Confronted with this problem of permanent correction of venous stasis where there is gross incompetence of perforators, we sought a means of controlling it mechanically. It is well known to every surgeon that the gross tissue changes due to venous stasis—namely, lymphedema, induration and fibrosis—may extend through the skin and the whole layer of subcutaneous tissue to the deep fascia, but these changes do not extend below it. The muscles are not edematous, are not indurated or chronically inflamed, and they are not fibrotic. In other words, they are not involved in the effects of venous stasis. If, then, it would be possible to move the deep fascia outside of the skin, presumably the skin and subcutaneous tissues would also be relieved of venous stasis.

To simulate the effect of deep fascia, a legging was constructed (Figure 8) with an inelastic outer casing and a thin bladder which, after it is in place on the leg, is pumped up by an automatically adjusting pump to 35 mm. of mercury pressure, which has in general been found to be optimal. By this method uniform pressure is applied to the skin throughout the extent of the legging. This is particularly important in the lower third of the leg where the contour is not circular. Also, the pressure during walking is a fluctuating one, undergoing cyclic changes with contraction and relaxation of the muscle, just as the pressure does normally in the muscular compartment below the deep fascia. So we have simulated moving the deep fascia outside of the skin and getting a fair share of this pumping action of the muscles on the veins contained within the deep fascia actually exerted against the skin and subcutaneous tissues.

Occasionally when the ulcer is below the malleolus we need to use a small accessory bladder, but I do not have time to discuss this aspect in detail. The theoretical basis for the air pressure method of controlling the venous stasis in the lower leg is a mechanical means of overcoming the adverse effects of venous stasis.

Now I will describe some results obtained with this method. A 28 year old pharmacist was seen a year ago because of lymphedema. He had had bilateral spontaneous thrombophlebitis 3 years ago. Two and a half years before we saw him he scraped his right ankle. He thought nothing of it at the time, but an open ulcer developed which did not heal. Two years before we saw him, an ulcer developed on the left leg, without any obvious trauma. He was treated by the usual type of compressive dressings, ACE® bandages, elastic stockings, and so on, and in spite of the best efforts, the appearance of his legs when he came to us was as shown in Figure 9.

Four months later, after applying the air pressure leggings, the upper parts of the ul-

cers were completely healed (Figure 10). The lower parts still showed open areas. Small foot bladders were applied in order to heal the lower parts, and 6 months after we started treatment, the appearance was as shown in Figure 11. The ulcers were completely healed.

At the present time the skin of his legs is in good condition. In the dependent position there is pigmentation, and the skin of the lower legs is bluish when he stands without the leggings.

I want to emphasize that treatment in this way, with air pressure, is operative only while the legging is being worn. It is a mechanical means of overcoming a mechanical defect.

A 46 year old man had bilateral thrombophlebitis following appendectomy. He had been a patient in our own clinic since 1937, and had been treated by ligations of perforators, saphenous ligation, injection, elastic compression and paste boots. Nearly everyone at our clinic had treated him at one time or other. In spite of that, when he was up and around, ulcers continued to develop and break down (Figure 12). Very often the ulcer is easily corrected when it first appears, but finally it becomes very refractory to treatment. He had had to give up his regular job as bus driver and was utterly discouraged; he had severe pain, and was on the point of going on relief.

His leggings were put on in September 1951. In 4½ months his legs were completely healed, and the photograph in Figure 13 was taken after 6 months.

There are 2 more cases that I would like

6

7

8

FIGURE 6 *(top)*. Typical postphlebitic state, left lower leg, showing venous stasis with induration, chronic inflammatory reaction, pigmentation and preulceration.

FIGURE 7 *(center)*. Stasis dermatitis with a weeping chronic inflammation of the lower leg typically much worse in the lower half.

FIGURE 8 *(bottom)*. Aero-pulse legging consisting of an inelastic casing fitted to the lower leg containing a thin bladder between the casing and the leg which is inflated with air by an automatically regulated pump to the optimal pressure (35 mm. mercury). This produces the physiologic effect on the venous return from the superficial veins of moving the deep fascia outside the skin and subcutaneous tissues.

FIGURE 9. Bilateral postphlebitic ulcers of the lower legs which had failed to respond to the usual elastic compressive methods of treatment.

FIGURE 10. Same patient as in Figure 9, 4 months after initiating treatment with aero-pulse legging. The upper parts of both ulcers have healed, but the portions of the ulcers below the malleoli have not completely healed.

FIGURE 11. Same patient as in Figures 9 and 10, 2 months later after adding to the aero-pulse legging the supplementary foot bladder which is occasionally required to heal ulcerations below the level of the malleolus. Both ulcers have completely healed.

FIGURE 12. A patient with postphlebitic stasis ulcers who was followed in our clinic for 15 years, a failure by the usual methods of treatment.

FIGURE 13. Same patient as in Figure 12. Ulcers were completely healed in 4½ months while the patient remained ambulatory and at work. These photos were taken 6 months after initiating treatment with the aero-pulse legging.

FIGURE 14. Stasis ulcers of both legs which had failed to heal firmly in 18 years.

to describe briefly. The first concerned a 65 year old man with large ulcers first on the right leg and then also on the left leg following the development of bilateral varicose veins and incompetent perforators. He probably had a phlebitis following a hernia operation 19 years earlier, and the ulcers had never healed completely in 18 years (Figure 14). This patient was sent to me from a distant city, and I was very frank with the man and told him I was not at all sure that the legging would heal his ulcer without skin grafting. After 4 months, the photograph in Figure 15 was made; the ulcer was completely healed. We put the legging only on the right leg in order to convince the patient that he would be improved. At the end of 2 months his right leg was so nearly healed that he wanted to have the left one treated also.

Postphlebitic lymphedema is illustrated in Figure 16, and I think the lesion speaks for itself. This woman had a very large ulcer in an area of postphlebitic induration, complete-

11a

12a

13a

14a

11b

12b

13b

14b

ly encircling the leg. In this case we felt that we would gain time by an immediate skin graft, which was done. Figure 17 shows the results at the end of 4 months. The legging was applied when she was first allowed up. All of you who have experience with skin grafting realize that in severe postphlebitic lymphedema you will often lose the skin graft when the patient is made ambulatory. We have had cases in which skin grafting was done as many as 8 or 10 times in postphlebitic lymphedema, and after use of this legging there has been prompt and permanent healing. This patient's leg has remained healed now for more than a year.

I had another case of this type, a compensation case, in which the patient had been

FIGURE 15 *(right)*. Same patient as in Figure 14, after 4 months of treatment with the aero-pulse legging on the right and 2 months on the left leg. The ulcers are practically healed on the right, markedly improved on the left.

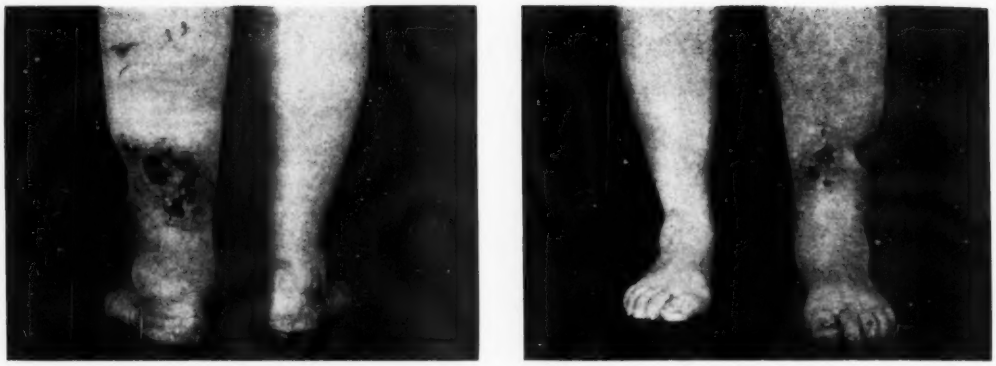

FIGURE 16. Extensive deep ulceration in a large area of postphlebitic induration encircling the lower leg.

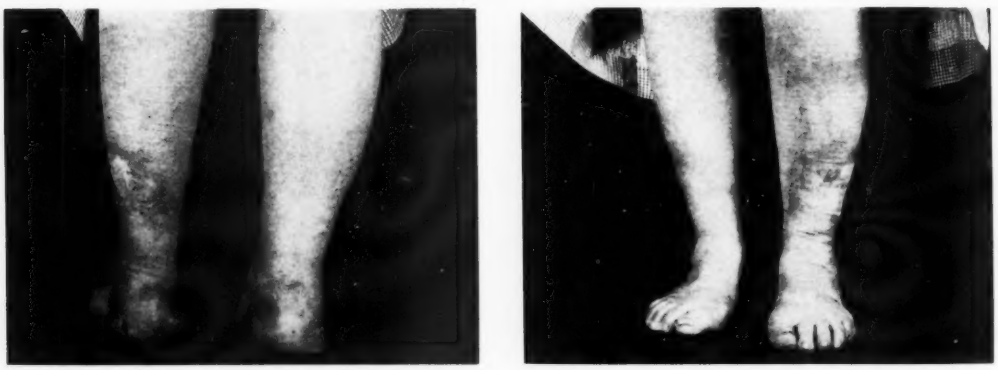

FIGURE 17. Same patient as in Figure 16. Result of excision of indurated area and split-thickness skin graft with immediate use of the aero-pulse legging on ambulation. The area was completely healed within a month with the patient ambulatory. This photograph shows the result at the end of 4 months, and the ulcer has not recurred.

in the hospital for a year and a half with multiple skin grafts in an attempt to get the ulcers healed; we were able to get our first graft to take permanently by putting on the air pressure legging immediately.

I want to emphasize, in closing, that this is a mechanical method of overcoming a mechanical defect. It is operative only while the apparatus is in place and being worn. You have to warn your patients of that, because after the ulcer is healed and the skin is in good condition, they feel very happy about it and forget to wear the legging. When there is severe venous stasis, as in these severe postphlebitics, if you are going to use this method of treatment you have to indoctrinate the patients to the effect that they must continue its use for the rest of their lives. In milder cases this is not true.

I don't want to leave you with the idea that all you do is put on the legging and everything is sweetness and light. I did not have time to go into the matter of dermatitis, which is the chief difficulty in the use of any covering of the leg, and that requires special treatment. But we have been able to take cases of stasis dermatitis that have not been relieved in any other way and finally, by carefully carrying them over the period of weeping, to clear them up entirely.

Transverse and Oblique Muscle-Splitting Abdominal Incisions

LOUIS T. PALUMBO AND IRVING A. KATZ*

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The anatomic and physiologic soundness of these incisions is compared with that of vertically placed pararectus or midline abdominal incisions. The results in 730 consecutive muscle-splitting or transverse abdominal incisions are discussed. The beneficial effects of early ambulation are presented. The infrequency of evisceration or incisional hernia in these types of incisions is contrasted with the higher incidence in vertically placed abdominal incisions.

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IRVING A. KATZ

THE great strides which have been made in abdominal and thoracic surgery during the past 40 years are well known and accepted by both medical and surgical groups throughout the world. Advances in technics, in preoperative and postoperative management and in use of antibiotics, whole blood and nonabsorbable sutures have gained widespread recognition and general acceptance. However, the use of newer types of abdominal or thoracoabdominal incisions, though anatomically and surgically sound, has not received the same degree of acceptance.

It is difficult to conceive that these types of incisions have not replaced, in most instances, the older and generally accepted vertical abdominal midline or paramedian incisions. These standard abdominal incisions have become so entrenched in usage that they continue to be the incision of choice in spite of the very favorable reports concerning muscle-splitting and transverse incisions which have appeared during the past 15 years.[1-30]

Vertical incisions may provide adequate exposure, but they are anatomically unsound. Injury to the nerve supply to the muscles is frequent. In a long incision of this type with splitting of the rectus abdominis muscle, 2 and frequently 3 intercostal nerves are damaged, resulting in atrophy and weakness of the wound. It has been shown that injury to one intercostal nerve is of no serious consequence because of the overlapping of the nerve supply by the adjoining nerve above and below, and therefore atrophy and weakness will not result. In making a vertical incision through the anterior and posterior rectus sheaths, the aponeurotic fibers are transected. In the closure of these sheaths the sutures are placed parallel to the direction

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of these fibers. Because of this fact and due to the lateral pull by the muscles of the abdominal wall, great stress is placed on the suture line which often results in tearing or pulling through of the sutures and weakening of the wound. This sequence of events has been observed by many surgeons who have attempted closure of the abdominal wall when the patient was under a light anesthesia.

Sloan[27] demonstrated actual strain coefficients on the suture lines of vertical incisions and showed the stress on the vertical wound to be proportionate to the square of its length. On this basis a geometric increase in the force exerted on the vertical wound occurs as the wound is lengthened, this force representing the combined pull and power of the transversus abdominis and oblique abdominal muscles. This force was 30 times greater in a vertical incision than in a transverse incision. A 30 pound force was necessary to approximate a 3 inch incision and an 80 pound force for a 5 inch incision. He also showed that the incidence of hernia varies as the square of the length of the vertical incision and that larger scars develop under wounds with greater tension. This pull is greatly enhanced by coughing and straining.

In a transverse incision or muscle-splitting incision, the lateral pull of the muscles of the abdominal wall will approximate the incision rather than pull it apart, thereby placing very little strain on the suture line and resulting in less pain and discomfort for the patient. The patient will be more cooperative in moving about in bed and in being ambulated early. Also, because of less incisional pain he will take deep breathing exercises and will cough more readily and thereby decrease the pulmonary complications. In closure of the rectus sheaths, which have been divided in a transverse direction, the sutures effecting approximation will pass across rather than parallel the heavy aponeurotic fibers, thereby making the closure more secure.

Sectioning of one or both rectus muscles transversely has no serious anatomic or physiologic consequences. There is no interference with nerve or blood supply. The muscle does not retract for any distance, since it is prevented from doing so by the tendinous bands which are normally present, attaching it to the undersurface of the anterior rectus sheath. In the reapproximation of the divided rectus sheath, the rectus muscle is likewise approximated and requires no suturing of this muscular layer. The healing process results in another tendinous band which does not impair the normal function of this muscle.

The blood supply to the abdominal wall is abundant. There is very little interference with this supply in a transverse or muscle-splitting incision. Therefore, delayed healing of the wound does not occur because adequate blood supply exists, and this supply is improved by early ambulation.[10,13,14,18] Delay in wound healing may occur due to depression of the blood supply by prolonged bed rest or immobilization.[10,14,18]

An incision is stronger during the first few days than from the fifth to the tenth postoperative days,[14,27] which is significant in determining the optimum time in ambulating the patient. Ambulation following major surgery during the first 24 to 48 hours appears favorable to wound healing, decreases the incidence of complications and does not increase the incidence of postoperative hernia or the risk of wound dehiscence.[8,10,13,14,18,20-23,26,29] These important features have been shown by many previous surveys.

The incidence of postoperative incisional hernias in vertical abdominal incisions is from 2 to 10 per cent. Incisional hernias and wound disruption are rare in transverse or muscle-splitting incisions. They usually do not occur unless the incision is complicated by a severe infection. A review of 9000 consecutive abdominal incisions by Singleton and Blocker[26] revealed an incidence of disruption in 1.02 per cent of 5,853 cases of vertical incisions as compared with 0.031 per cent in 3,147 cases of muscle-splitting or transverse incisions. The postoperative hernia rates were 2.24 per cent and 0.92 per cent, respectively. Rees and Coller[25] in 225 consecutive transverse incisions reported 1 small hernia, which developed at the site of drainage. Perworth[24] in 1946 reported no hernias in 480 cases of transverse abdominal incisions. Whitaker and

associates[30] in 1949 reported 1000 consecutive cases of transverse abdominal incisions (65 per cent of these cases were trauma or acute pathologic conditions of the abdomen) with wound disruption in 9 cases, an incidence of 0.9 per cent. Singleton and Blocker[26] in a review of 762 of their cases of upper abdominal incisions revealed an incidence of wound disruption of 3.08 per cent in 292 vertical incisions as compared with none in 470 transverse incisions. The hernia rate was 5.4 per cent in the former group and 0.21 per cent in the latter.

The complication rates are also significantly reduced, as evidenced by the results reported in the literature when both groups of incisions were studied. Rees and Coller[25] showed a marked reduction in the rate of pulmonary complications in their series of 571 cases; in the group of 225 cases with transverse incisions the rate was 2.6 per cent as compared with 9.5 per cent in the group of 346 cases with vertical incisions. These complications and many others can be further reduced by early ambulation.[13,14,20-23,29]

Types of Incisions and Results

This report is based on a study of 730 consecutive muscle-splitting or transverse abdominal incisions employed during the past 6 years.

The incisions included in this study are as follows: 220 transverse elliptic supraumbilical and infraumbilical; 273 transverse midabdominal to the right or left of the umbilicus; 163 subcostal, right or left; 47 oblique suprainguinal, left; and 27 thoracoabdominal, right or left (Table 1 and Figure 1).

The transverse supraumbilical and infraumbilical incisions were performed by dividing the anterior and posterior rectus sheaths and both rectus abdominis muscles in a transverse direction. The deep superior and/or inferior epigastric vessels, as the case may be, were ligated and divided. The peritoneum was incised, likewise, in a transverse direction. These incisions provide adequate exposure to the upper (supraumbilical) and lower (infraumbilical) abdomen.

The closure of the incision was accomplished in layers, using single interrupted 00 silk sutures in the anterior and posterior rectus sheath layers and 000 silk in the subcutaneous and skin layers. In this series of 297 cases wire was utilized in only 2 patients.

The exposure obtained in the supraumbilical type permitted easy access to all the structures and organs of the upper abdomen, so

TABLE 1

ABDOMINAL MUSCLE-SPLITTING INCISIONS

TYPE	NUMBER	PER CENT
Supraumbilical, transverse	203	27.8
Infraumbilical, transverse	17	2.3
Subcostal, right or left	163	22.4
Transverse midabdominal, right or left	273	37.4
Suprainguinal, oblique, left	47	6.4
Thoracoabdominal, right or left	27	3.7
TOTAL	730	100.0

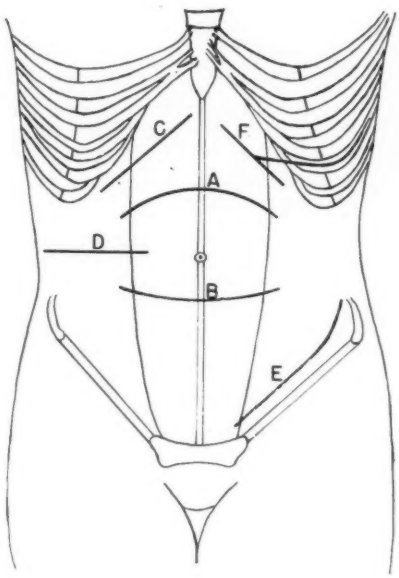

FIGURE 1. Abdominal incisions. A. Supraumbilical, transverse. B. Infraumbilical, transverse. C. Subcostal. D. Transverse midabdominal. E. Suprainguinal, oblique. F. Thoracoabdominal.

that major procedures of considerable scope were performed without hindrance. The surgical procedures performed through this incision were 194 partial or total gastrectomies, 1 pancreatectomy and 8 partial colectomies. The same type of incision placed below the umbilicus in 17 cases permitted the performance of various types of pelvic surgery and total colectomy.

The average age of the patients in the supraumbilical group was 48 years and that for the infraumbilical group was 32 years. In both these groups 57.7 per cent were ambulatory within 24 hours, whereas the remaining number were ambulatory after the sixth postoperative day.

Dehiscence and incisional hernia did not occur in these cases. There were 2 wound complications, consisting of infection and hematoma.

The subcostal incision was employed in 163 cases. Of this number 147 were for cholecystectomy, 9 for splenectomy and 7 for partial colectomy. The average age in this series was 48 years. Seventy-two per cent of the patients were ambulatory within 24 hours. There were 10 wound infections, an incidence of 6.1 per cent. All of these occurred in the gallbladder series. Two patients developed small incisional hernias at the lateral edge of the wound, an incidence of 1.3 per cent. There were no cases of dehiscence.

The incision for the subcostal approach was placed 2 to 3 inches inferior to the left or right costal arch. The anterior and posterior rectus sheaths and the right or left rectus muscle, as the case may be, was transected obliquely. If additional exposure was required, the external and internal oblique and transversus muscles were split in the direction of their fibers. The incisions were closed in layers with silk, except in 2 cases in which wire was used.

The transverse midabdominal incision was performed in 273 cases. Of this number 236 were for a right or left lumbar sympathectomy, 17 for partial or hemicolectomy, 6 for resection of terminal ileum, and 14 for ileotransverse colostomy. The average age of the patients in this group was 49 years. Seventy-eight per cent were ambulatory within 24 hours. Infection of the wound occurred in 2.9 per cent and hematoma in 1.5 per cent of the cases. Dehiscence did not occur. An incisional hernia developed in 1 case, an incidence of 0.37 per cent. Silk was the suture material, except in 7 cases in which wire was used and 8 cases in which catgut was employed.

The skin incision was transverse, placed at the level of the umbilicus; the medial edge began about 3 inches from the midline and extended lateralward to the lateral body wall. The skin flaps were mobilized superiorly and inferiorly in order to expose a broad expanse of the underlying muscles of the anterior abdominal wall. The external oblique aponeurosis and muscle were split in the direction of their fibers and separated from the underlying internal oblique muscle. This latter structure and the transversus muscle and fascia were likewise split in the direction of their fibers. The anterior and posterior rectus sheath were not disturbed. If the operation to be performed was intraperitoneal, the peritoneum was then incised in the vertical direction. If a retroperitoneal procedure was to be accomplished, the extraperitoneal fat and peritoneum were freed from the lateral and posterior body wall and were then displaced upward and medialward.

The closure of the incision was done by suturing the muscles in separate layers with interrupted silk.

The left oblique suprainguinal incision was employed in 47 cases. Of this number 14 were for abdominoperineal resections; 31 for anterior resection of portions of the left colon, sigmoid, or upper rectum, and 2 for ileosigmoidostomy. The average age of the patients in this group was 53 years. Sixty-four per cent were ambulatory in 24 hours. Dehiscence occurred in 1 (0.21 per cent) patient on the tenth postoperative day. He was a 71 year old man on whom an abdominoperineal resection was performed. The incision was closed with silk. The dehiscence most likely was a result of wound infection. In this group there were 2 wound infections and 1 hematoma. There were no cases of postoperative hernias. All incisions were sutured

with silk, except for 12 closed with wire and 3 with catgut.

The skin incision for this series was made parallel and a few inches superior to the left inguinal ligament; it extended from the midline, upward and lateralward to the left flank. The external oblique aponeurosis was split in the direction of its fibers. The internal oblique and transversus muscles were split in the direction of their fibers. If additional exposure was necessary, the anterior and posterior rectus sheaths and left rectus abdominis muscle were divided transversely. The peritoneum was opened in an oblique manner. This provided a wide exposure to the pelvis and left side of the peritoneal cavity. The closure of the incision was carried out in layers using interrupted silk sutures.

In the last group, a combined thoracoabdominal incision, right or left, was employed in 27 cases. Of this number, 17 were for total or partial gastrectomy, 2 for resection of the lower esophagus, 2 for cholecystectomy, 3 for portal-caval anastomosis and 3 for splenectomy with reefing of esophageal varices. The average age of this group was 48 years. Eighty-five per cent were ambulatory in 24 hours. Three cases developed wound infection. There were no cases of dehiscence or incisional hernias. The incision was closed with interrupted silk sutures.

In this combined incision the abdominal portion was performed first in order to permit an exploration to determine operability and/or the type of surgical procedure to be carried out. The abdominal portion of the incision was placed about 3 inches inferior to the costal arch extending from the midline obliquely to the outer limit of the rectus abdominis muscle. The anterior and posterior rectus sheath and rectus muscle were divided in an oblique manner. If a decision was made to perform extensive surgery, the skin incision was then extended upward across the costal arch in the sixth, seventh, eighth or ninth intercostal space, as required. The costal arch was divided with a knife, and the intercostal bundle of muscles was likewise divided equidistant to the adjoining ribs. The incision was carried to at least the anterior or midaxillary line. The pleura was divided and the left or right thorax entered. The diaphragm was then divided in a radial manner from its attachment to the chest wall down to the esophageal hiatus on the left, or to the central tendon on the right, as the case may be. This provides a wide exposure of the lower thorax and upper abdomen. The incision was closed in layers with interrupted silk sutures, including the diaphragm. An intercostal tube drainage was provided through a stab wound at a lower level to drain the thorax.

In the total series of 730 cases, the average age was 47 years; the oldest patient was 73 and the youngest 24 years of age. Fourteen per cent of these patients were more than 60 years of age. The average follow-up was 28 months, the shortest being 3 months and the longest 5 years. In over 78 per cent a follow-up was obtained. Of the remaining number, 16.7 per cent were not followed and 5.3 per cent died as a result of terminal malignancy or surgery prior to the first 3 month follow-up. Seventy per cent of the patients were ambulated within 24 hours. Infection of the incision developed in 24, or 3.3 per cent, of the cases, and hematoma of the wound in 6, or 0.82 per cent.

Dehiscence occurred in only 1 case, an incidence of 0.14 per cent. Three (0.41 per cent) postoperative incisional hernias developed (Table 2).

Silk was the suture material used in closure of the incision in 95.5 per cent of the cases, wire in 2.9 per cent, and catgut in the remaining 1.6 per cent.

Comment

The transverse or oblique muscle-splitting abdominal incisions are anatomically, physiologically and clinically sound. The incision is so placed as to provide adequate exposure with minimal trauma to the nerve and blood supply of the structures of the abdominal wall. It affords opportunity for extension of the original incision, should this prove necessary. This type of incision produces a narrow, firm cicatrix which is comfortable during convalescence, and therefore the patient moves about more freely in bed and is able to be

TABLE 2

SUMMARY OF RESULTS IN TRANSVERSE AND OBLIQUE MUSCLE-SPLITTING ABDOMINAL INCISIONS

TYPE	NUMBER	(PER CENT)	AVERAGE AGE	AMBULATION		WOUND COMPLICATIONS		DEHISCENCE	INCISIONAL HERNIA
				Early	*Late*	*Infection*	*Hematoma*		
Supraumbilical and infraumbilical, transverse	220	(30.1)	40	125	95	1	1	0	0
Subcostal, right or left	163	(22.4)	48	118	45	10	0	0	2
Transverse, midabdominal, right or left	273	(37.4)	49	213	60	8	4	0	1
Suprainguinal, oblique, left	47	(6.4)	53	30	17	2	1	1	0
Thoracoabdominal, left or right	27	(3.7)	48	23	4	3	0	0	0
TOTALS	730		47	509 (69.8)	221 (30.2)	24 (3.3)	6 (0.82)	1 (0.14)	3 (0.41)

ambulated early with safety. These latter factors are important in reducing the complications, particularly pulmonary, following major abdominal surgery. The closure of these multimuscular-fascial-aproneurotic layers with a nonabsorbable suture material assures a safe and solid wound. These patients experience less pain and therefore require less sedation and narcosis. The rehabilitation of the patient is more rapid and his hospital stay shortened considerably.

As has been shown in this report and from the reports in the literature, the incidence of wound and other complications are significantly reduced by these types of incisions when compared with the less favorable results occurring in the commonly employed vertical abdominal pararectus or midline incisions.

The incidence of dehiscence and incisional hernias is markedly reduced when a muscle-splitting abdominal incision is employed. In fact, the 1 case of dehiscence in this series occurred in an old patient who developed a severe wound infection following bowel surgery. Two of the 3 hernias in 730 cases were small and insignificant when compared with the usual large ventral hernias seen following vertical abdominal incisions.

Summary

The transverse or oblique muscle-splitting abdominal incision is a sound procedure providing adequate exposure and minimal damage to the nerve and blood supply of the structures of the abdominal wall; also, it is placed in the lines of normal stress and strain. Thus, the patient experiences less discomfort and is more cooperative in early postoperative management, which aids in reducing complications and results in a more rapid ambulation and rehabilitation of the patient.

The incisional closure is performed by a multiple layer technic of nonabsorbable sutures across the normal aponeurotic and muscle fiber bundles, providing greater strength in closure and less strain on the suture line because muscle pull is parallel to the line of incision rather than at right angles to it.

All these factors are more favorable in reducing the incidence of eviscerations and herniations.

A series of 730 consecutive transverse or oblique muscle-splitting abdominal incisions employed for a great variety of major surgical procedures is presented. The average age of the group studied was 47 years; 509 of these

patients were ambulatory early and 221 ambulatory late. Dehiscence occurred in only 1 case, an incidence of 0.14 per cent. Incisional hernias occurred in 3 cases, or 0.41 per cent. This low incidence of 2 important incisional complications is significantly less than those reported for vertical abdominal incisions.

Early ambulation of 70 per cent of these patients resulted in more rapid rehabilitation and a marked reduction in hospital stay.

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NEW BOOKS RECEIVED

New books received are acknowledged each month. As space permits, books of principal interest to our readers will be reviewed more extensively. Reviews and additional listings will be found in this issue starting on page A-78.

The Obstetrical Forceps. By L. V. Dill, M.D., Head, Obstetrics and Gynecology, Yater Clinic, Washington, D.C. 156 pages, 91 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $5.25.

A Guide to Medical and Dental Photography. By Kenneth S. Tydings, S.P.E. 124 pages, illustrated. 1953, Greenberg, Publisher, New York. $1.95.

Antibiotics. By Robertson Pratt, Ph.D., Professor of Pharmacognosy and Plant Physiology, University of California College of Pharmacy; and Jean Dufrenoy, D. Sci. (Paris) Research Associate in Antibiotics, University of California College of Pharmacy, San Francisco. Ed. 2. 398 pages with 87 illustrations. 1953, J. B. Lippincott Company, Philadelphia. $7.50.

Current Research on Vitamins in Trophology; Proceedings of the Scientific Sessions of the Eighth Annual Meeting, The National Vitamin Foundation, Incorporated, New York. Edited by Robert S. Goodhart, M.D. 157 pages, illustrated. July, 1953, The National Vitamin Foundation, Incorporated, New York. $1.50.

Disability Evaluation; Principles of Treatment of Compensable Injuries. By Earl D. McBride, M.D., Assistant Professor in Orthopedic Surgery, University of Oklahoma School of Medicine, Norman. Ed. 5. 715 pages, illustrated. 1953, J. B. Lippincott Company, Philadelphia. $15.00.

Human Embryology. By Bradley M. Patten, Professor of Anatomy, University of Michigan Medical School, Ann Arbor. Ed. 2. 798 pages with over 1400 drawings and photographs. 1953, The Blakiston Company, Inc., New York and Toronto. $12.00.

Respiratory Diseases and Allergy. By Josef S. Smul, M.D., Fellow, National Gastroenterological Association. New York. 1953, Medical Library Company, New York. $2.75.

PRELIMINARY REPORT

Use of Nylon Mesh in Repair of Abdominal Wall Defects

BENEDICT B. LANDRY*

St. Francis Hospital, Hartford, Connecticut

NYLON® *mesh has been used in 11 cases for repair of abdominal wall defects. It seems to have all the advantages of tantalum mesh with the added features that it is not subject to "metal fatigue" or "work hardening" and that it is more substantial with less extensibility. Also, it remains intact and becomes impregnated with fibrous tissue without fragmentation. It is much less expensive than tantalum, and up to the present probably is the most satisfactory of all the prostheses used in repair of abdominal wall defects.*

THE repair of large abdominal wall defects has for many years tried the ingenuity of surgeons. Various methods of repair have been introduced. These defects for the most part are complications of surgery for various abdominal conditions and result from wound weakening, wound rupture and wound infection. They occur also in persons who are systemically debilitated.

Difficulty in effecting repair is also encountered in cases of large inguinal hernias, whether indirect, direct or of the sliding type. In these the deficient quality of the tissues or the tremendous suture tension resulting from attempts at repair causes doubt as to a satisfactory outcome. Another problem in repair concerns voluminous hernias which have been considered *noli me tangere;* in these cases the patients are almost totally incapacitated.

Fascial transplants and flaps, pedicled muscle, vulcanized rubber, VITALLIUM® and silver plates (German), silver filigree, stainless steel cloth and cutis grafts all have been used with variable results, none with uniform success. Some surgeons state that they can repair almost any defect of the abdominal wall with combinations of fascial flaps and catgut or other suture material; it is difficult to conceive how their results could be uniformly successful in some cases of massive hernia we have encountered.

Welch[1] reported on a method of Ziffren and Womack for the repair of huge inguinal hernias. The hernia is reduced by means of a long, relaxing abdominal incision into which the abdominal contents are allowed to bulge. Only the skin is approximated. About two weeks later this new abdominal hernia is repaired. It would seem that simplification is offered by the use of nylon mesh in a one stage procedure as compared with this two stage operation.

Since 1944, when nylon mesh was first used in France, tantalum mesh has been used in repair of large abdominal wall defects and of large and recurrent inguinal hernias. Up to the present time this has seemed the most efficient of the various methods. Throckmorton,[2] Dunlop[3] and Koontz[4,5] have employed it in many cases with good results. Douglas[6] of the Royal Infirmary of Edinburgh has also used tantalum mesh or gauze, as it is also called, and has carried on considerable research on the subject of repair of hernial defects. Through him our acquaintance with the

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use of nylon mesh, also called crinoplaque and nylon-thread mesh, was first obtained. He gave the impression of great enthusiasm for the use of the nylon mesh, which was introduced by Acquaviva and Bourret[7] in a paper read before the Surgical Society of Marseilles, France, in June 1944. To Acquaviva is credited the original idea for the use of nylon mesh in the manner to be described.

Nylon mesh (22 by 100 mm.) is about the same size as tantalum, and is sterilizable, but its method of use varies somewhat. There is little difference in tensile strength, but nylon is more substantial, equally supple and malleable and hence just as easy to handle. One feature claimed by the French school of surgeons after it had been used in many cases is that there is no fragmentation such as occurs due to "metal fatigue" in the case of tantalum and steel mesh. Reoperation has been done subsequent to the implantation of nylon mesh, and the abdominal wall found to be almost as suturable as a normal one, the plaque having remained intact.

Nylon mesh is available in any size desired, the most common being from 6 by 9 cm. to 14 by 21 cm. It is advisable to have various sized sections on hand to take advantage of the selvage edges and hence prevent fraying of the mesh.

Those who have used tantalum mesh extensively do not report any great difficulty because of fragmentation due to "work hardening," but it is obvious that the material which remains in one piece would be preferable, if the same fibrous tissue reaction occurs in each case.

Our experience with the use of nylon mesh has not been extensive (a total of 11 patients), but we feel that the attention of American surgeons has not been directed sufficiently to its use in treatment of abdominal wall defects. We first used it in March 1951, to our knowledge for the first time in this country, in a poorly nourished man with a large incisional hernia of the upper midabdomen which had developed after exploration for a chronic pancreatic condition (Case 1, Table 1).

Nylon is used similarly to tantalum, with the exception that the nylon edges are not folded over, and that the mesh is countersunk below the fascial planes for at least ¾ inch. Tantalum mesh is folded and sewn to the edges of the fascia (although recent reports mention the omission of folding and some writers specifically state that they no longer fold the tantalum edges). Retaining sutures may be silk, cotton, steel alloy, nylon or tantalum strands. We recommend metal suture material because of the occasional occurrence of wound sinuses with the use of silk. Some French surgeons fix the nylon at four or five cardinal points, believing that after intimate contact with the tissues and the early tissue reactions the mesh stays in place. We have felt more secure in using suture attachments freely. Rigid hemostasis and asepsis are absolutely essential in the use of either tantalum or nylon, as indeed in all surgery.

BENEDICT B. LANDRY

As is the case in the use of tantalum mesh, the old scar or scars are excised and the skin margins freed in all directions until intact fascia, or as near normal fascia as can be found, is encountered. This is undermined for approximately 1.5 to 2 cm. so that the nylon mesh can be countersunk. It is advisable to attain perfect hemostasis of the operative field at this time. The peritoneum is then opened and all adhesions separated and all adherent bowel loops restored to normal relationships. After removing any excess, the peritoneal layer is closed. Whenever possible, as much of the fascial planes as can be approximated without tension are sutured together. The nylon mesh is then cut to the desired size for filling the defect or, better still, a piece as nearly the accurate size as possible with the selvaged edges intact is attached by countersinking with interrupted sutures a distance of 1.5 to 2 cm. beneath the fascial planes.

Drainage by means of perforated polyethylene tubes beneath the skin is instituted after instillation of penicillin solution into the area, and the skin margins are approximated, with any excess of skin being removed

TABLE 1

SUMMARY OF 11 CASES OF ABDOMINAL HERNIA IN WHICH NYLON MESH WAS USED IN REPAIR

CASE SEX AND AGE	TYPE OF HERNIA	DATE OF OPERATION	DATE OF FOLLOW-UP	RESULT
1* M 37	Incisional, upper abdomen	March 1951	April 1952	Good
2 F 57	Incisional, upper midabdomen	July 1951	August 23, 1952	Good
3 M 70	Bilateral, direct inguinal	September 1951	August 11, 1952	Good
4 M 51	Incisional, right rectus	November 1951	August 1, 1952	Good
5 M 48	Left inguinal. Primary treatment by injection	December 1951	September 10, 1952	Fair. Abdominal wall fine. Wound sinus
6 M 76	Umbilical and ventral. Latter repaired with nylon	February 1952	†	
7 F 55	Incisional, intestinal obstruction. Resection	March 1952	September 20, 1952	Good. Persistent small wound sinus
8 F 51	Pfannenstiel incisional. One previous attempt at repair	May 31, 1952	September 10, 1952	Good
9‡ F 51	Voluminous incisional and ventral	July 7, 1952	September 22, 1952	Good
10 F 66	Incisional, upper right rectus	July 28, 1952	September 19, 1952	Good
11 M 47	Large direct inguinal	August 11, 1952	September 10, 1952	Good

*Figures 1a, b and c.
†Died March 13, 1952, of uremia.
‡Figures 2, 3a and 3b.

if this previously has not been done.

Acquaviva and his colleagues use glass drainage tubes for 48 hours, keep the patients in bed for two weeks, and place sand bags over the abdominal area involved to eliminate dead spaces and promote early intimate reaction between the mesh and cellular tissues. It is stated that at first there is an inflammatory reaction with many polymorphs and that after a few months there are foreign body giant cells with connective tissue. Later the fibrous tissue predominates and is definitive in the repair, cells becoming incorporated in the nylon mesh. In one of our cases (Case 1, Figures 1a, b and c) we removed a segment of the abdominal wall approximately one year after insertion of nylon mesh. The tissue was quite resistant to the cutting blade. The pathologic report follows:

Macroscopic—Specimen consists of two wedge-shaped pieces of firm tissue, each containing a mesh of fine firm fibers.

1a

1b

1c

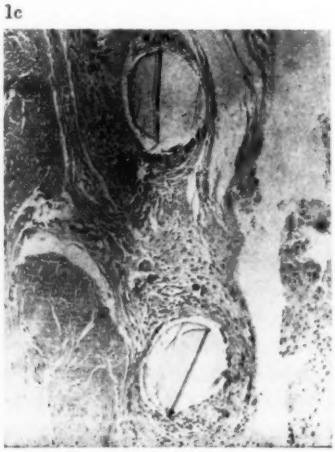

FIGURE 1*a* (Case 1). Anterior view one year after hernial repair. Scar with sutures represents area where tissue was removed for microscopic examination. *b.* Lateral view. *c.* Low power photomicrograph of tissue specimen removed.

FIGURE 2 (Case 9). Anterior view of large incisional and ventral hernia. The excoriated areas and the ointment used to heal them can be seen. This patient was quite obese. Because of the weight of the hernia and the multiple skin excoriations, she was almost a helpless invalid. It was necessary to hospitalize her for a prolonged period prior to operation in order to heal the excoriations and reduce her weight by 35 pounds.

FIGURE 3*a* (Case 9). Anterior view four months after operation. *b*. Lateral view.

Microscopic—Sections are composed of formed connective tissue which is fascia and proliferating fibroblastic new connective tissue. Running through this background are two types of fibers which are cut in cross section. The first type is a pale blue homogeneous material which is said to be nylon. About these fibers there is excellent fibrosis, fibroblastic reaction and healing, without evidence of irritation, inflammation or foreign body reaction. The second type of fiber is obviously silk suture and about this is the customary inflammatory and foreign body reaction.

Complications

In Case 8 there was profuse drainage of thin, murky, amber-colored fluid for approximately three weeks after pressure dressings were removed. This drainage decreased abruptly, leaving a small sinus at one end of a Pfannenstiel incision which gradually closed.

The patient in Case 10 had a large upper right incisional hernia. There was discharge of clear, watery fluid for about 10 days. The patient was allergic to adhesive plaster and we feel that intimate contact with the tissues was not adequately obtained at first by the swathe dressings used. The area repaired in this case has been firm, as in all the cases.

A peristent sinus in the middle of a lower abdominal incision was a feature of Case 7. The sinus was explored and several knots and loose pieces of silk were removed, resulting in diminution but not complete cessation of the discharge which was scanty and viscid in character.

Another patient (Case 5) has a troublesome sinus in the outer end of an incision for repair of a large hernia which had been treated elsewhere by injection. Two attempts at repair had been made before we used nylon mesh. In this case we are inclined to blame the extremely poor quality of the tissues, which did not completely hold the edges of the nylon, allowing shredding of part of the mesh and constituting localized foreign body reaction.

From our experience, we believe that to prevent these complications it is essential (1) to maintain drainage for seven to eight days, using small caliber, perforated polyethylene tubing placed laterally beneath the skin and over the sewn combined mesh and fascial layers; (2) to use sand bags over the area for 10 to 14 days as stressed by Acquaviva in order to maintain intimate contact of the tissues and nylon planes. In our first patients we followed this practice and the result was healing *per primam* with very little drainage; (3) to use metal or alloy suture material to obviate any foreign body reaction such as occurs occasionally with silk.

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The Value of Operative Cholangiography

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The authors are dissatisfied with the current indications and results of common duct exploration for stones. In an effort to improve the results of biliary tract surgery, a series of consecutive cases using operative cholangiography were studied. This paper describes experiences encountered in the development of a good technic for operative cholangiography and the results obtained by the method. The advantages and limitations of operative cholangiography are discussed.

ALBERT BEHREND

RECENTLY we reviewed the fate of the patient with retained stones in the biliary ducts and analyzed the morbidity and mortality which accompanies this surgical catastrophe.[1] One result of the investigation was that it clearly pointed to the inadequacies of the usual criteria for exploration of the ducts. When the common bile duct was opened, stones were too often missed, only to be demonstrated on *postoperative* cholangiography, much to the chagrin of the surgeon and to the detriment of the patient. We then determined to perform operative cholangiography on a consecutive series of patients requiring biliary tract surgery. The purpose of this paper is to evaluate an admittedly limited experience with operative cholangiography, to discuss our successes and our failures and to present a technic which has proved generally satisfactory.

One outstanding result of this investigation was the finding that in the past, on the basis of clinical indications alone, 25 per cent of common ducts were explored, whereas, using operative cholangiography in addition to clinical indications, 65 per cent of ducts were opened.

Clinical Indications for Common Duct Exploration

Our indications for exploration of the common duct in the past were the following:

1. Increased diameter of the duct.
2. Thickening of the duct walls.
3. History or presence of jaundice.
4. Numerous small stones in the gallbladder.
5. Dilated cystic duct.
6. Palpation of stone in the common duct.
7. Cholangitis.
8. Pancreatitis or induration of the head of the pancreas.

On the basis of these criteria the common bile duct was explored in 25 per cent of the patients operated on during a 5 year period from 1946 to 1951.

During this investigation we were surprised

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to find stones and gravel in ducts considered clinically normal in size. That there are normal variations in the diameter of the common duct became plainly evident. We routinely palpated the ducts for stones, but where stones were found on exploration, they were infrequently felt. We do not feel that the inability to palpate a stone in the ducts constitutes a valid reason for not exploring them, if other indications exist.

Contraindications to Operative Cholangiography

Pride in our ability to determine which common ducts required exploration and which did not, and to remove all the stones when the duct was open, was for years a deterrent to our use of operative cholangiography. That such pride was false was determined by *postoperative* cholangiography all too often. The recent study by Corff, Berger and Gershon-Cohen[2] from our hospital showed retained stones in 9 (18 per cent) of 50 consecutive cases in which *postoperative* cholangiograms were done. These operations were performed by staff and resident surgeons and the results are comparable to those reported by others (Thiessen,[3] Hughes, et al.[4]).

Another deterrent to the use of operative cholangiography was the feeling that too much time would be consumed. From the standpoint of patient safety, prolonged operating time is no longer a serious factor, thanks to improved anesthesia. However, in the hospital where full schedules tax operating room facilities, it may be an important consideration. We feel that we have overcome this objection so that it is not unusual for us to do a needle cholangiogram, cholecystectomy, choledochostomy, and T tube cholangiogram with closure of the abdomen within 45 minutes of the time of incision. The method whereby this is accomplished will be discussed subsequently.

Actually, time may be saved by the utilization of operative cholangiography. On many occasions prior to its use, we explored the duct, removed stones, and then searched with probes sometimes unsuccessfully for many additional minutes, fearful that another stone or stones might remain undetected. (Sometimes they were, as shown by *postoperative* cholangiograms.) The time wasted in fruitless probing and, perhaps more importantly, the trauma caused by the search are both avoided by the ability to take a cholangiogram immediately after the T tube has been sutured in place.

The additional cost to the patient may be considered a valid contraindication. When the reasons for the operative cholangiogram were discussed with the few patients who questioned the charge, no further objection was raised. It is easy to justify a $25 x-ray fee when the patient knows it may prevent prolonged hospitalization or even reoperation.

In no case have we felt that wound infection or delayed healing resulted from the use of x-ray apparatus in the operating room.

Technic of Operative Cholangiography

Operative cholangiography requires the cooperative efforts of surgeon, anesthetist and roentgenologist. Until this is obtained, errors will occur as we discovered in our first cases. Probably similar failures have discouraged other surgeons from using the method.

The middle section of the operating table pad is removed and a wooden tunnel substituted. The patient is then placed in position on the table so that the biliary track and duodenum are judged to be in the field of a 10 by 12 inch x-ray film. The first film may be inserted in the tunnel at this time. Inhalation anesthesia is induced with PENTOTHAL SODIUM® and continued with intratracheal nitrous oxide-oxygen plus 5 per cent intravenous DEMEROL®. The operative field is prepared and draped and the abdomen is opened. The presence of stones in the gallbladder is determined and the cystic duct, hepatic duct and common bile duct are exposed. The cystic duct is clamped, and distal to the clamp a needle attached to a syringe containing 15 cc. of 35 per cent DIODRAST® is inserted. We prefer to use a 19 gauge needle* which can be readily bent to conform to the course of the duct. A rigid steel needle will break after several bendings, tends to slip out of the duct, and is more likely to pierce its back wall.

*Supplied by Becton, Dickinson Company, Rutherford, New Jersey.

The plunger of the syringe is withdrawn to aspirate bile from either the cystic duct or the common duct. Ten cubic centimeters of 2 to 20 per cent procaine hydrochloride are injected into the common duct to overcome any spasm which may be present at the sphincter of Oddi. This is followed by the injection of 15 cc. of 35 per cent Diodrast. Pads and retractors are removed from the wound, which is covered with a sterile towel, and the portable x-ray apparatus is wheeled into position.

The anesthetist then introduces succinyl choline chloride 0.15 per cent by intravenous drip until complete apnea occurs. This agent is rapidly metabolized by the body so that normal respiration is restored within 2 minutes. However, the anesthetist uses artificial respiration by pressure on the bag of the machine as soon as the x-ray film is exposed. Momentary apnea is an absolute necessity, for without it a clean outline of the ductal system will not be obtained.

FIGURE 1 *(left)*. Operative needle cholangiogram discloses a stone in the common bile duct. Clinically there was no reason to suspect common duct stone, and the duct was normal in size. Diodrast flows into the duodenum readily. Such a stone, if not detected, could cause obstructive jaundice or postcholecystectomy syndrome subsequently.

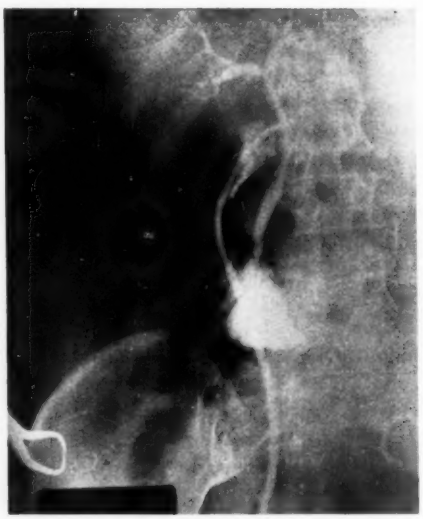

FIGURE 2a *(left)*. Operative needle cholangiogram in a patient who had had a severe attack of acute pancreatitis 10 days previously. The shadows of multiple (60) small stones are seen in the distal common duct. Note the reflux of Diodrast in the pancreatic duct. This could have been the mechanism which produced the attack of acute pancreatitis. b *(right)*. Operative T tube cholangiogram after removal of the common duct stones. Note that reflux into the pancreatic duct no longer occurs.

At a signal from the anesthetist, the film is exposed for 1 to 3 seconds using a 25 ma., 75 K.V. portable apparatus. The film is removed from the cassette holder and immediately developed. This takes approximately 5 to 7 minutes and during this time the gallbladder may be removed. If there are obvious clinical reasons for opening the common duct it may be done before removing the gallbladder and while the film is being developed. Hepatic and common ducts are explored with probes, scoops and forceps, and flushed with saline. A probe is passed through the ampulla into the duodenum. On several occasions, stones have been removed before the exposed film was returned to the operating room. A T tube is sutured into the common duct and usually a watertight closure is obtainable. Another film is slipped into the tunnel, 15 cc. of 35 per cent Diodrast is injected and the film is exposed repeating the technic outlined. While this film is being developed, the gallbladder and/or the appendix may be removed. Closure of the abdomen is then accomplished. If the second film shows residual stones, the abdominal incision is readily reopened. If the picture is satisfactory, closure of the abdomen may be accomplished by the time the developed film is read.

Analysis of Clinical Material

During the past few months, 34 consecutive patients with gallbladder or biliary tract disease had operative cholangiograms. This is a number admittedly too small to have statistical significance but not too small to teach lessons of practical value.

In 12 cases, the cholangiogram showed no evidence of obstruction and dye entered the duodenum promptly. In these, the common duct was not opened. In 22 cases (65 per cent), the common duct was opened. Stones

FIGURE 3a *(left)*. Operative T tube cholangiogram shows dye entering the duodenum readily. There is no evidence of stone. b *(right)*. Postoperative cholangiogram (7 days) shows a stone in the common bile duct. It disappeared after 2 weeks of modified Pribram therapy. Operative cholangiography is not infallible but has greatly reduced the number of retained common duct stones.

FIGURE 4a *(left)*. Operative needle cholangiogram shows many stones in the common duct and the hepatic ducts. Little dye has entered the duodenum. b *(right)*. Operative T tube cholangiogram shows no stones in the common duct but many residual stones in the inaccessible hepatic ducts. We believe this is an indication for transduodenal sphincterotomy, which was done in this case to permit stones to pass with greater ease subsequently.

were removed in 14 of these and no stones were found in 8. Most of the latter cases must be considered as technical failures. Failures have become less frequent as experience is gained. The causes of failure have been (1) improper positioning of the patient over the film, (2) inability of the anesthetist to control respiratory motion, (3) injection of the dye around the duct rather than into it and (4) spasm of the ampulla of Vater causing false positive evidence of obstruction.

Of greater significance are 3 cases in which operative cholangiography showed no obstruction but in which stones were present and undetected. In 2 cases the duct was opened despite apparently normal needle cholangiogram because clinical indications for doing so were present. Stones were removed in both cases. In a third case, needle and T tube operative cholangiography revealed no block, but a cholangiogram made 7 days after the operation showed a stone at the ampulla. This disappeared after 2 weeks of treatment by procaine-ether and alcohol drip modification of Pribram's method. These false negatives (10 per cent) show that the method is not infallible. However, by combining clinical indications for opening the common duct with cholangiographic evidence, unsuspected stone was left in the common duct only once (3 per cent). In other cases, inaccessible stones in the secondary hepatic ducts have been detected at operation and transduodenal sphincterotomy has been performed to permit subsequent passage of these stones.

Conclusions

1. Clinical and operative criteria are not sufficiently reliable in determining the need to explore the common bile duct.

2. After opening the common bile duct and removing the stones it is impossible to be certain that residual stones do not remain in the biliary tract.

3. Operative cholangiography gives the surgeon another weapon to help him determine which duct to open and whether stones remain after exploration.

4. The method is not infallible. The usual clinical criteria for opening the common bile duct should not be discarded. Operative cholangiography should be used as an adjunct and not as the sole method of determining which ducts should be opened.

5. Close cooperation of the surgeon, anesthetist and roentgenologist is a necessity in developing a good technic. The means of obtaining this has been described.

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Transthoracic Dorsolumbar Sympathectomy

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A surgical technic for transthoracic dorsolumbar sympathectomy is described which has been found to supply the answers to many of the technical problems involved in this procedure. It is not reported as a new concept in technic, and a review of the numerous surgical methods for sympathectomy has therefore been deliberately excluded. It appears that an ever increasing number of surgeons are employing a transthoracic approach to the sympathetic nervous system, and the described procedure is presented as that preferred.

W. P. KLEITSCH

THE following is a description of an operation which permits maximum exposure of the sympathetic nervous system as well as an easy approach to the adrenals. With this procedure it is possible to expose for manipulation the entire sympathetic nervous system from D2 to L2, including the splanchnic nerves and celiac ganglions. It permits exposure, for examination or resection, of the adrenal glands and of the superior pole of the kidney. It is a procedure, therefore, which permits a maximal exposure of all structures involved in sympathetic nervous system surgery.

Anesthesia

The anesthetic agent is not particularly important, but general anesthesia administered through an endotracheal tube is essential. A continuous intravenous infusion is maintained throughout the operation to help control blood pressure. Although the first stage of this operation offers no problems unusual to an ordinary thoracotomy, the second stage is often associated with unusual anesthesia problems. Indeed in the second stage of this operation the anesthesiologist becomes an integral part of the procedure. It is important, therefore, that a physician well experienced in anesthesiology be in attendance. The specific problem encountered in second stage dorsolumbar sympathectomy is neurogenic shock resulting from bilateral excision of the sympathetic nervous system. It is the responsibility of both the anesthesiologist and the surgeon to determine how to maintain an adequate systolic blood pressure during this phase. Blood transfusions are needed only in small amounts since blood loss is usually small. It is generally unwise, therefore, to attempt to restore blood pressure by transfusions. Vasopressors are more strongly indicated, and these are administered by the anesthesiologist as required. Norepinephrine is the ideal vasopressor, although NEOSYNEPHRINE® is a valuable and considerably less expensive substitute.

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Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

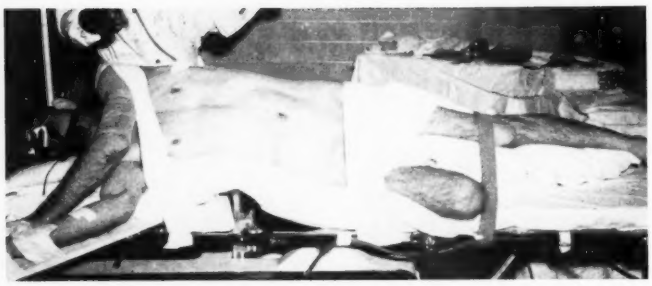

FIGURE 1 a *(left)*, b *(below, right)* and c *(below, left)*. The position on the operating table. Note the following points: elevator under short ribs; arms held extended on board with adhesive tape; position of legs with pillow for support. The adhesive tape over the shoulders and hips maintains the proper degree of rotation. The usual incision is used.

Position

This is a two stage operation, since each side is done in the lateral decubitus position. The patient is placed on the operating table with the kidney elevator under his short ribs. His hands and arms are extended on an arm board and held in place by an adhesive tape band. The kidney lift is elevated until the chest forms a gently convex surface. The shoulders are secured in position by means of a wide adhesive tape band passing over them and fastened to the operating table on each side. The shoulders are rotated backward to form a 70 degree angle with the tabletop. A pillow is placed between the legs, and the lowest knee is flexed under it and the upper leg extended on it. The legs are held in position by means of a canvas strap fastened just above the knee. Finally the hips are rotated backward to an angle of approximately 70 degrees with the top of the table and fixed, as were the shoulders, with a wide adhesive tape band (Figure 1).

This position permits a wide thoracotomy exposure, tightens the psoas muscle on the side which is to be operated on and permits

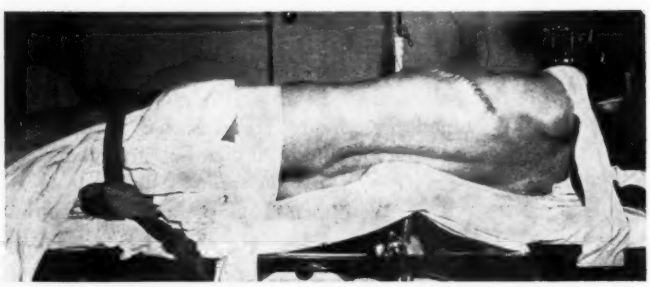

FIGURE 2 *(right)*. Mobilization of the pleura to expose the thoracic sympathetic chain. Only a sufficient amount to expose the nerve elements is elevated.

access to the dorsal surface of the lumbar vertebrae. The operator stands behind the patient and works upward during the thoracic phase and downward during the lumbar portion.

Incision

The incision is ordinarily planned for the region of the eighth rib. It is better to use an incision which will give the best approach in the individual case than to be concerned with arbitrary anatomic localization. In short, obese individuals it may be necessary to use the ninth rib, and in long, slender persons the seventh rib might be better. The best site for the incision is usually the crest of the thoracic convexity, which is identified after the patient is positioned on the table.

The selected rib is exposed through an anterior thoracotomy incision and resected subperiosteally from the cartilage to the angle. Trauma to the chest wall is reduced as much as possible by cutting only as much of the latissimus dorsi muscle as is needed for exposure, and by bluntly separating the digitations of the serratus anterior muscle. The exposed rib is first freed anteriorly by cutting through its cartilaginous portion; it is then mobilized posteriorly and divided with a rib shears in the vicinity of the angle. The thorax is entered through the periosteal bed of the excised rib. Warm, moist pads are applied to the wound edges and the incision is opened by means of a rib spreader. The lung is collapsed by the pressure of warm, moist pads.

Dorsal Sympathectomy

The thoracic sympathetic system is dissected out first. With the chest opened and the lung collapsed the dorsal sympathetic chain is readily identified in its entire length. An incision is made in the parietal pleura parallel to and immediately lateral to the sympathetic chain, extending from the first to the tenth rib at which point the pleural incision then curves anteriorly over the body of the vertebra (D10) to the region where the greater splanchnic nerve disappears into the diaphragm (Figure 2).

With a long, toothed forceps, a Smithwick dissector and a long scissors, the pleura is mobilized medially, exposing the sympathetic chain and the splanchnic nerves. Mobilization of the pleura should be limited to that amount which is necessary to expose the nerve elements. Oozing from the retropleural space is controlled by warm, moist compresses. The only active bleeding which may develop will follow injury to the intercostal vessels and is controlled with hemostatic clips.

The sympathetic chain is now grasped by long, curved forceps (hysterectomy clamps) at the point where the greater splanchnic nerve arises. With mild traction on the forceps the sympathetic chain is freed by dividing the anterior and posterior communicating rami with scissors. Care must be taken in this process, especially in obese subjects, to avoid injuring the intercostal veins. These veins are pulled up by traction on the rami and may be injured unless adequate care is taken. Bleeding from a lacerated intercostal vein, although seldom serious, is annoying, since the operation must be interrupted to close the leak.

The dorsal chain may be mobilized up into the neck. At the second rib special care should be taken to avoid injuring the first intercostal vein (Figure 3). Dissection in this area may be somewhat tedious because it is quite removed from the incision. For this reason bleeding can be doubly annoying; however, control by hemostatic clips is always possible and assures positive hemostasis. The use of GELFOAM® is not considered safe unless the pleura can be sutured over the Gelfoam to

FIGURE 3 *(left)*. Exposure of the thoracic sympathetic system obtainable with this approach.

FIGURE 4 *(below)*. Diagrammatic representation of the lumbar phase of the operation. A retractor has been inserted through the diaphragmatic incision and is elevating the retroperitoneal fat as well as the liver and adrenal (dotted outline). Traction on the greater splanchnic nerve by the forceps exposes the celiac ganglion. The dissector has separated the fibers of the crus and is mobilizing the second lumbar ganglion.

hold it in place. Dissection of the upper end of the sympathetic chain is, of course, indicated only when radical excision is planned.

After the first intercostal vein is passed, the dissection can be carried into the lower neck if desired, and the chain may be divided as high as the stellate ganglion. Stellate ganglionectomy should be avoided because of the consequent development of Horner's syndrome and the undesirable effects of a postganglionic sympathectomy.

A specially modified clip-applying forceps has been designed for working high in the chest in this operation. With ordinary clip-applying forceps the operator's vision is obscured by the back of his hand. The forceps recommended have a curve in the handle similar to the Sweet clip-applying forceps and a curve in the beak similar to the Smithwick forceps. The first curve removes the hand from the line of vision, and the second curve brings the tip of the instrument into direct view. This instrument has been found to be invaluable in this operation and has been described elsewhere.

After the upper end of the chain is divided, mobilization of the lower thoracic segment together with the splanchnic nerves can proceed apace. Little difficulty is encountered until the region of the twelfth dorsal ganglion is reached. Here the chain will all but disappear. It becomes extremely thin, and is buried in the muscle fibers of the diaphragmatic pillar, and great care must be taken to insure that it is kept intact. An intact chain is a distinct help in locating the lumbar ganglions. Mobilization of the dorsal sympathetic chain and splanchnic nerves down to the diaphragm completes the first half of the operation.

Lumbar Sympathectomy

To complete this phase of the procedure the operator must change his position so that he can work downward through the thoracotomy. A modified Henrotin vulsellum forceps (Figure 6) is used to grasp the tendinous portion of the diaphragm a little behind the dome. Traction on the forceps will then

flatten the curve of the diaphragm and partially immobilize it. This maneuver exposes the posterior portion of the costophrenic sinus. A finger is then inserted along the vertebral column, parallel and immediately next to the greater splanchnic nerve, and an opening is developed through the diaphragm and into the retroperitoneal space. An incision is made anterolaterally in the diaphragmatic pleura extending from the opening developed by the finger out toward the dome and, by continuing tension on the finger, an opening in the diaphragm can be developed largely by separating its muscle fibers. In this manner few blood vessels will be injured, and the troublesome bleeding which follows transection of the diaphragm is largely avoided. Bleeding vessels in the diaphragm are best secured by suture ligature.

After the diaphragm has been divided for about one-third of its diameter, the retroperitoneal space can be entered. The adrenal gland and kidney may be explored both by palpation and under direct vision. The adrenal gland is readily available to the surgeon for section if adrenalectomy is indicated. If an adrenal tumor is suspected, the subdiaphragmatic portion of the operation may precede the thoracic portion.

By the judicious use of moist packs and retractors, the retroperitoneal fat can be held out of the field and off the lumbar vertebra (Figure 4). Traction on the greater splanchnic nerve will help identify the celiac ganglion which is readily available for dissection. The splanchnic nerves can now be detached from the ganglion, or part or all of the ganglion can be excised. Attention is then directed to following the sympathetic chain from the twelfth thoracic ganglion down to the first lumbar segment. This is the most difficult part of the procedure since the chain is very thin in this area and is easily torn. The first lumbar ganglion, furthermore, is extremely inconstant and is absent more often than it can be demonstrated.

However, with care the sympathetic fibers can be traced through the muscle fibers of the crus of the diaphragm, and the second lumbar ganglion can always be found. Demonstration of the third lumbar ganglion may be attended with some difficulty in obese individuals and it cannot regularly be included in the dissection. Care should be taken to prevent damage to the lumbar veins. Although a bleeding lumbar vein usually can be controlled by the application of clips, if the vein retracts into the retroperitoneal fat an additional flank incision may be needed for sufficient exposure to obtain hemostasis. This, however, is rarely necessary.

Closure

Following division of the lumbar sympathetic chain at the desired level, the entire surgical specimen can be removed as one piece (Figure 5). Hemostasis is assured and closure then begins with suture of the diaphragm. Interrupted 0 cotton sutures have been found to be very satisfactory for this purpose.

The parietal pleura is sutured in its most accessible (lower) portion. A running lock stitch of 00 chromic catgut is most conveniently used for this purpose. The upper portion of the pleural incision needs no sutures. A de Pezzer catheter is inserted through a stab wound in the fifth interspace in the anterior axillary line, the chest is irrigated with warm saline solution and the thoracotomy wound is

FIGURE 5. The surgical specimen of a radical sympathectomy, showing the entire dorsolumbar system intact from D2 to L2 as well as a portion of the celiac ganglion.

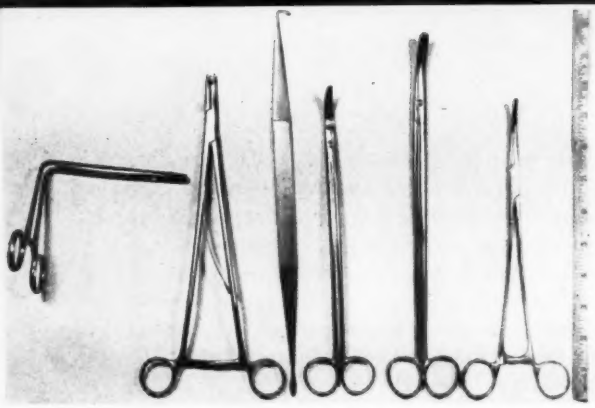

FIGURE 6. Useful instruments for this operation. From left to right, a Henrotin vulsellum forceps with a 90 degree bend in the handles for traction on the diaphragm; a modified Sweet-Smithwick clip-applying forceps; Smithwick nerve hook and dissector; Satinsky thoracotomy scissors; 11½ inch Willauer scissors, and Sarot intrathoracic artery clamp.

closed. A continuous 00 chromic catgut suture for closure of all layers of the chest wall has been found to be adequate. The skin is closed with a running nonabsorbable suture. The lung is inflated before completion of the operation and the patient is returned to his room where the chest tube is connected to a water seal bottle.

Discussion

The operation described is a radical, two stage sympathectomy. It is not the purpose of this communication to justify this procedure but rather to describe an operation which permits a maximum attack upon the structures involved in sympathetic nervous system surgery.

A transthoracic approach to the sympathetic nervous system appears logical and desirable. The most common complication of retropleural sympathectomy is a pleural tear. By approaching the sympathetic nervous system transpleurally one takes full advantage of an opened pleura and gains maximum exposure. Furthermore, by opening the thorax deliberately the surgeon is well prepared to take the necessary steps to insure a complete re-expansion of the lung and elimination of postoperative hydrothorax.

The instruments used are standard sympathectomy and thoracotomy instruments with some rather minor modifications (Figure 6). The modified instruments are readily available from any surgical instrument manufacturer without excessive cost.

The most serious objection to the operation is that it is a two stage procedure. Although most patients will accept the staged procedure, there is little doubt that a one stage operation would be more desirable. However, since the operation is done transpleurally and in the lateral decubitus, the two stage procedure is accepted as being part of the price of a better exposure and a more complete operation.

FIGURE 7. Postoperative appearance of thoracotomy scars.

DIAGNOSTIC CLINIC

Acute Nonbacterial Gastroenteritis

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A minor illness is described which is present continuously in the population. From the data presented and from more detailed data which are in the process of publication, the conclusion can be drawn that the gastrointestinal tract of man is subject to bombardment with a nonbacterial agent in a manner very similar to that in which the upper respiratory tract is assailed by the agents of the common respiratory diseases.

It is highly probable that each and every one of you has at one time or another suffered from acute nonbacterial gastroenteritis. This condition has been discussed sporadically in the medical literature under such headings as acute gastroenteritis, epidemic nausea and vomiting, epidemic diarrhea, and the winter vomiting disease. It has been dealt with in the lay press under such terms as intestinal "flu" or virus X. It is a familiar disease of the hospital population, particularly of the intern and nursing staff, and here its etiology is invariably laid to the parsimony of the hospital director. Examination of a normal population over a period of time, however, discloses that instead of its being a sporadic epidemic disease, as reports of institutional outbreaks would indicate, acute gastroenteritis is a disease which is always with us.

This article is based on such a population study. For approximately 5 years the Department of Preventive Medicine at Western Reserve University has been following a group of normal Cleveland families. These families are observed as closely as the traffic will bear. Each mother keeps a day-by-day record of the symptoms—respiratory, gastrointestinal and others—that are noted in each member of the family. A field worker visits each family every week and checks the mother's record and takes blood cultures and other necessary specimens. Whenever an illness occurs, even a very minor one, a physician from the department visits the home, examines the ill person and classifies that illness clinically to the best of his ability. Twice a year each person included in the study is subjected to a physical examination which includes x-ray, blood count, urinalysis and serologic testing. Thus, as you can see, this population is observed intimately.

The findings of the first 3 years of this study have been analyzed, and it is apparent that acute gastroenteritis is an important source of morbidity. Acute respiratory diseases accounted for about 75 per cent of illnesses. Acute gastrointestinal upsets comprised 15 per cent, and the remaining 10 per

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cent were the childhood diseases and various ailments and injuries.

The clinical picture of acute gastroenteritis deserves some comment, although you all may be familiar with it. To the four major symptoms—fever, abdominal pain, vomiting and diarrhea—may be added headache, dizziness, various degrees of abdominal cramps and what some of the subjects have described as abdominal uncertainty. The individual attack by no means always includes all these symptoms; for instance, from our observations it has been noted frequently that whereas some members of a family may have a full-blown attack, others may suffer from one loose stool or just a few abdominal grumblings.

The onset of the attack usually is quite abrupt and, although parents may not believe it, is not more frequent at night than in the daytime. Symptoms vary with the age of the patient. In young children, vomiting is common, whereas in adults the disease tends to produce less vomiting and more diarrheal symptoms. The average duration of an attack is 48 hours, and when symptoms persist much longer than that, another diagnosis should probably be suspected.

Hospitalization because of acute gastroenteritis is rarely required, although parents should always be warned of the dangers of dehydration. The few fatalities caused by this disease have occurred in cases where the symptoms of dehydration were ignored long.

The differential diagnosis is of considerable importance in that a number of other conditions can simulate this disease closely—or, perhaps more accurately, this disease can simulate other more serious illnesses. In this particular geographic locality (Cleveland) we are not too concerned about differentiating between acute or nonbacterial gastroenteritis and bacillary dysentery, but in some areas this may be quite difficult. As Dr. Hardy and Dr. Watt of the Public Health Service have pointed out, many cases of bacillary dysentery are extremely mild and could easily be mistaken for acute gastroenteritis. One differential point is that in the latter, the appearance of blood or frank pus in the stool is very rare.

Food poisoning is another differential point. Again, by clinical appearance alone one would have great difficulty in differentiating between food poisoning—*Salmonella* infection, in other words—and acute nonbacterial gastroenteritis. But on epidemiologic grounds this differentiation can always be made. Frequently the nonbacterial illness will begin as an attack in one individual and then appear after 24 hours or so in other members of the family, which is not usually the case in food poisoning. Also, when one is confronted with the problem of the disease occurring simultaneously in several members of the same family, often one can find a history of mutual exposure to another family suffering from this disease.

An important illness in regard to differential diagnosis is streptococcal sore throat. As Dr. Joseph Brennemann emphasized long ago, streptococcal sore throat may give rise to severe abdominal pain and vomiting, and if the patient is less than, say, 4 years old and is unable to complain of sore throat, the differential diagnosis may be difficult in the presence of fever, abdominal pain and vomiting. Since the need is great for early treatment of acute streptococcal sore throat in order to prevent to the greatest possible degree the development of such complications as acute rheumatic fever, the differentiation from acute gastroenteritis is most important. In any patient who appears more ill than would be expected in a case of simple gastroenteritis, careful observation of the throat and cervical glands is always indicated.

The other condition to be differentiated from acute gastroenteritis, of course, is acute appendicitis. It is difficult to describe all the differentiating features, but I think one can rely most on epidemiologic evidence. If a child or an adult has acute abdominal pain, a mild elevation in temperature and vomiting, and appendicitis is suspected, the presence of vomiting, diarrhea or nausea in other members of the family will aid in excluding appendicitis from consideration.

It is of some interest that in our study we have observed about 1 case of appendicitis to some 450 cases of acute gastroenteritis.

A few remarks are in order concerning the

natural history of the disease. Its incidence is quite high; it would appear that almost every adult has 1 attack a year and that each child suffers from 2 or possibly 3 attacks a year. The seasonal distribution is also of considerable interest, the attack rate being low during August and July with a sharp increase in September and the highest rate throughout the winter months. This distribution suggests that immunity to this illness must be transient, in that each autumn finds the population a fertile ground for reinfection, and that the causative agent must be present almost all the time.

The condition is similar to common respiratory diseases in that children are afflicted much more frequently than adults. Infants are protected from the disease and have a relatively low attack rate, but this increases year by year progressively until the child is 5 years of age and then gradually declines, suggesting again that over the course of years a relative immunity develops.

Since this is a common disease, one obviously is interested in the mode of transfer of the agent. From the symptoms it would be expected that there is an enteric spread; however, there is no evidence to back up this assumption. Certainly the seasonal distribution is diametrically opposite to what one would expect in an enterically transferred disease. Then, too, one would expect that if this disease were spread by the fecal-oral route, the mother, who is usually the food handler, would spread the disease more rapidly throughout the family than would the father or one of the children. That, also, is not so.

In considering the possibility of respiratory spread, one again runs up against a blank wall. A certain number of affected persons, perhaps coincidentally, have respiratory symptoms, but those persons do not spread the illness any more readily than others who have no sneezing, coughing or nasal discharge. As is the case with the common cold, children spread it to one another more readily than they do to adults or than adults spread it to children. So one comes to the rather unsatisfactory conclusion that close personal contact appears to be necessary for spread of the disease, a situation analogus to that found at present in poliomyelitis and also in infectious hepatitis.

Because it is a self-limited disease, a wide variety of treatment methods have been recommended. Since one can count on a 48 hour course, I think perhaps the best form of therapy is the administration of fluids by mouth in very small amounts. This can be done by encouraging the child to drink with the aid of a teaspoon, and to do it slowly. Extreme thirst is a feature of the illness, and if the patient suddenly takes a large drink of fluid, that fluid will promptly return. If diarrhea is severe and vomiting relatively less so, perhaps paregoric will be of some help.

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CASE REPORT

Bleeding Ulcers May Perforate

LOUIS PELNER* AND WALTER PUDERBACH**

Swedish Hospital, Brooklyn

The medical aphorism or maxim, "Bleeding ulcers do not perforate," is a menace to the practice of medicine, since it may cost the life of a patient.

LOUIS PELNER

WALTER PUDERBACH

THE medical aphorism, "Bleeding ulcers do not perforate and perforated ulcers do not bleed," is still quite generally accepted by physicians and surgeons, in spite of rather impressive evidence that both of these disastrous events can occur in the same patient, often at the same time. Although concomitant bleeding and perforated ulcer in the same patient are fortunately rare, the denial of the possibility of their occurrence may cost the life of the patient. Gordon-Taylor[1] has classified these associated catastrophies into 3 groups: (1) hemorrhage and perforation occurring concomitantly, (2) hemorrhage following a recently treated perforation and (3) perforation occurring while the patient is being treated for hemorrhage. The patient to be described belongs to the last category.

Case Report

A 50 year old man was first admitted to the Swedish Hospital of Brooklyn on July 8, 1952, with a history of epigastric pains for more than 20 years. A gastrointestinal x-ray series done a year previous to admission had revealed a duodenal ulcer. Two days before admission, he had severe epigastric pain radiating to the left and upward into the chest. He had taken large amounts of alcohol for several days before the onset of the pain. This pain was unlike that previously experienced, in that it was not relieved by food and was in an unusual location.

Physical examination revealed tenderness over the left upper quadrant of the abdomen as well as a positive Murphy test on the left side. Because of the unusual location of this pain, acute pancreatitis was considered a possibility. Serial amylase figures were 310, 470, 245 and 148 units at 4 day intervals. Under BANTHINE® therapy the pain subsided rapidly. A gastrointestinal x-ray series taken before discharge showed a spastic duodenal bulb with a deep ulcer niche (Figure 1).

The patient did well at home for more than 6 months. He was readmitted on January 10,

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1953. He gave a history of vomiting a small quantity of blood 2 days before this admission. One day later he vomited very large amounts of blood and had several jet black stools. He collapsed and was in obvious shock. He was given 1500 cc. of blood before evidence of recovery was seen.

Blood was present in the stool for the ensuing 10 days, but was slowly diminishing in amount. His condition 10 days later was good. The stool showed +1 occult blood, the hemoglobin was 12.6 gm., and the red blood cell count was 4,010,000 at that time.

The following day he vomited slightly, but there was no blood in the vomitus. He did not take food that day. That evening he had a sudden onset of severe epigastric pain, and he passed a small amount of bright red blood at stool. His pain increased markedly, and the abdomen became rigid. The patient became disoriented. His condition was discussed with several colleagues who emphatically stated that bleeding ulcers do not perforate. His condition was poor, so that he was operated on at once.

At operation large amounts of free blood were found in the abdominal cavity, and a large mass of blood clot and free blood was noted in the lesser omental space. There was a large area of induration in the pancreas and in the third portion of the duodenum, and a perforation of the posterior superior wall of the duodenum, ¼ inch in diameter, was noted 1 inch proximal to the ligament of Treitz. The perforation was distal to the ampulla of Vater and for this reason gastric resection was not done. The blood and blood clots were evacuated, the perforation was closed and omentum was sutured over the ulcer bed. His postoperative course was satisfactory and he was discharged 10 days later. He was to be admitted subsequently for definitive surgery.

Comment—This patient has had peptic ulcer for years. His first admission was for acute pancreatitis, undoubtedly caused by irritation from a penetrating duodenal ulcer on the posterior wall, although the possibility of an alcoholic debauch as the cause of the pancreatitis cannot be eliminated. His second hospital admission was for massive bleeding, presumably from a duodenal ulcer. While being treated for this condition and doing very well by all clinical tests, a perforation suddenly developed. There is presumptive evidence available that the perforation occurred in the ulcer that had previously bled, because the peritoneal cavity was filled with free blood and clots rather than gastric contents. Also, on the evening that the ulcer perforated, the patient passed a small quantity of red blood by rectum. The perforation was on the posterior superior surface of the third portion of the duodenum. His original ulcer noted on the first admission was in the first portion of the duodenum (Figure 1). Multiple ulcers, in which one may bleed and another may perforate, have been noted in the same patient. In our patient, we feel that the same ulcer both bled and perforated.

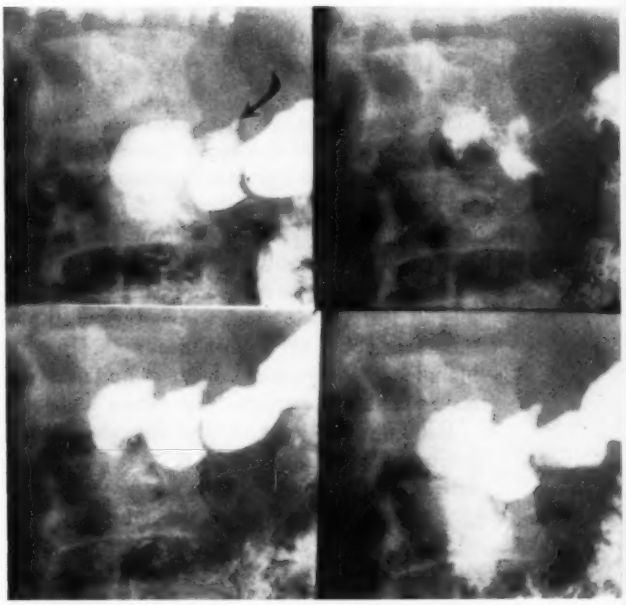

FIGURE 1. Polygraph showing spastic duodenal bulb with deep ulcer niche in first portion of the duodenum.

Discussion

The old axiom, "Bleeding ulcers do not perforate and perforated ulcers do not bleed," has been subscribed to by many famous physicians,[2-6] notably Behrend[2] and Einhorn.[3] They independently showed by anatomic dissection that the location of most perforated ulcers, i.e., the area immediately around the pylorus, possesses a deficient circulation. They noted that the arteries in the submucosa in the pyloric region of the lower lesser curvature of the stomach are practically terminal vessels and are sparsely distributed, thus allowing only a limited blood supply to the area. These arteries are also subject to repeated forcible contractions of the interlacing muscular bundles of the pyloric ring, which further limits the circulation to the pyloric area. In this bloodless area perforations are quite apt to occur, and hemorrhage least likely to occur.

Behrend[2] also stated that the ulcers that perforate are chronic, hard and indurated with a firm connective tissue base, while the ulcers that bleed are acute, soft and congested with very few connective tissue elements. He stated emphatically that he had never seen a case that both perforated and bled. While there may be some logical theoretical reasons for this fact, if we can prove that one ulcer only is present in each patient, there is no reason why both types cannot be present in a patient at the same time. This actually has been noted numerous times in the literature.[7] In our patient it is most certainly true that the same ulcer both bled and perforated.

Gordon-Taylor[1] divided the patients with concomitant perforation and hemorrhage into 3 groups, because the prognosis varied rather widely. In those cases where there were simultaneous perforation and hemorrhage, a gastrectomy was done, and all the patients recovered. When the hemorrhage preceded the perforation, as in our case, all the patients that were seen died, whatever the type of treatment. He claimed that this was because the enfeebled condition of the patient masked the ordinary clinical picture of perforation. Finally, all of his patients who bled after a successful operation for perforation died. Others have been more fortunate with the latter complication,[8,9] but where hemorrhage has preceded perforation the results of treatment have been usually uniformly poor.

Baker[10] in a review of bleeding peptic ulcer stressed the difficulty of diagnosis when hemorrhage precedes perforation. He considered that sudden collapse of a patient under treatment for bleeding was usually due to further hemorrhage, but on some occasions this may be due to perforation. He stated that persistent pain after bleeding should alert the surgeon to a possible perforation even if the abdominal signs do not entirely support the diagnosis.

In a recent paper, Gordon-Taylor[11] quoted Avery Jones in the statement that severe pain persisting after hemorrhage is a bad prognostic sign, and surgical treatment is urgently indicated if a perforated ulcer is not to be missed.

Thus it would seem that the advice given in the aphorism, "Bleeding ulcers do not perforate and perforated ulcers do not bleed," has been completely disavowed. On the contrary, the physician should search diligently for signs of perforation in every patient whose resistance has been lowered by massive hemorrhage.

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GENERAL PRACTICE *Review*

This department offers the latest, proved methods for the treatment and management of commonly encountered conditions based on the extensive experience of the physicians who prepare these summaries for POSTGRADUATE MEDICINE.

Complications of Myocardial Infarction

ROBERT W. OBLATH AND GEORGE C. GRIFFITH*

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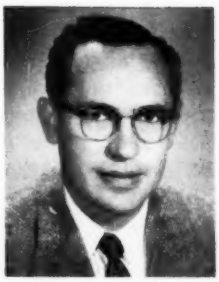
DEFINITIVE measures in the treatment of myocardial infarction are usually directed against the complications of this condition. It is the purpose of this paper to review these complications and methods for treating them. They are discussed in the general order of their appearance after the onset of infarction.

GEORGE C. GRIFFITH



ROBERT W. OBLATH

Shock

Shock is the most important immediate complication. Its mechanism is not agreed upon, but it is generally considered to be due to reduced cardiac output, reflex peripheral circulatory failure with impaired venous return to the heart, or a combination of both. It is reported to occur in 15 to 50 per cent of all patients who suffer acute myocardial infarction. The mortality rate is from 75 to 90 per cent as compared with a death rate due to all causes in myocardial infarction of 20 to 25 per cent. The condition is recognized by a hypotension of less than 80 mm. of mercury systolic for one hour or more in a previously normotensive patient, or of less than 100 mm. of mercury systolic in a previously hypertensive patient. In addition, there are the clinical manifestations of peripheral circulatory collapse.

The longer the duration of shock the worse is the prognosis. Various reasons have been advanced as to why this is true, but one of the most tenable is that during the period of shock coronary blood flow is so reduced that the remaining myocardium suffers further damage, and finally the patient passes into an irreversible stage from which he cannot recover. It is evident that the chances of spontaneous recovery are uncertain and risky.

Treatment consists of the usual measures of position, warmth, oxygen and morphine or

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other suitable narcotics. In addition, sympathomimetic amines are invaluable. These agents have decreased the mortality due to shock by about 50 per cent. Noradrenalin (LEVOPHED®) is our agent of choice in the usual case. It is administered as a continuous intravenous drip at a rate adjusted to maintain blood pressure at the desired level. A convenient method of administration is as follows:

Because veins are usually collapsed or may collapse, a polyethylene catheter is inserted into the vein either through a suitable large-bore needle or by means of a cut-down; it is then left in place either until the patient is out of shock and in a stable state or until he dies in intractable shock or from other cause. An ampule of noradrenaline (4 mg. per ampule) is diluted in 500 or 1000 cc. of distilled water and is administered as a continuous intravenous drip. The rate of flow is set at that necessary to bring and maintain the blood pressure as nearly as possible at a normal level. *Frequent blood pressure determinations must be made; this necessitates constant medical and nursing observation.*

When the patient appears to be out of shock and in a stable state, as shown by the need for smaller amounts of noradrenalin, the drip may be temporarily discontinued. In order to keep the tubing open for subsequent emergencies, a slow drip of 5 per cent glucose is maintained through the opposite arm of a Y tube. The important complications of such therapy are phlebitis and slough, but, because of the gravity of the situation, these should not deter from treatment.

A number of patients will not respond to this regimen; there is evidence that cortisone will potentiate the effects of noradrenalin in these instances. The cortisone should be administered parenterally in doses of 50 to 100 mg. or more daily. The usual precautions must be observed relative to sodium retention and potassium depletion.

Methoxamine hydrochloride (VASOXYL®), mephentermine sulfate (WYAMINE®) and phenylephrine hydrochloride (NEO-SYNEPHRINE®) are useful agents and reports of their beneficial results have appeared. They are limited in that they are not as well suited for continuous intravenous drip as is noradrenalin, are too rapidly metabolized for intermittent use, and, at least with the first two, lose their effectiveness relatively early in shock. They are excellent for emergencies and may be lifesaving while awaiting either transportation to the hospital or preparation of an intravenous setup. Neo-synephrine is used intravenously in doses of 2 to 7 mg.; methoxamine and mephentermine are administered intravenously in doses of 5 to 15 mg. These medications alone may be all that are needed in certain patients just going into shock or in mild shock; blood pressure in these patients may return to and stay at normal levels. If they are unsuccessful, noradrenalin should be used without hesitation. In some instances judicious use of several of these agents in combination may be required.

Because of its effects on heart rate and blood pressure in patients with heart block, isopropylnoradrenaline (ISUPREL®) is of particular importance in shock associated with heart block.

Epinephrine, ephedrine, caffeine and other vasoconstrictor drugs have been advocated at various times, but these agents have distinct limitations and are of little or no use at the present time.

Blood or plasma by vein or artery has been advocated. This method alone is inferior and results are poor. These agents may be useful adjuvants, however, but should be given cautiously. Amounts of 100 to 250 cc. at a time are usually recommended. The exact amount given and the speed of administration are usually determined by the needs of the particular patient.

Oxygen is a most important agent. Arterial oxygen saturation averages about 94 per cent in normal individuals. It has been shown that the saturation is decreased to about 80 per cent in patients with shock or pulmonary edema. Hence, oxygen may be critical. It may be given by tent, nasal catheter or mask.

Tents are the most comfortable to the patient and give moderate concentrations of oxygen (40 to 60 per cent), but they are the most expensive to buy and operate. The high-

est concentrations of oxygen can be obtained by the use of masks; these have the disadvantage that they must be fitted tightly and cannot be tolerated by some patients. Concentrations of 75 to 100 per cent may be obtained at flows of 6 to 12 liters per minute. The cheapest method of administering oxygen is by means of nasal catheter. A nasal catheter will give oxygen concentrations of only 30 to 40 per cent and therefore is not recommended. A nasopharyngeal catheter is recommended and will yield 45 to 70 per cent concentrations at oxygen flows of 6 to 8 liters per minute. The distance from the external nares to the tip of the ear lobe should be measured; the catheter is then passed through the nose into the oral pharynx this distance or until the patient begins to swallow. It is then withdrawn slightly and secured in position. Oxygen should be used continuously while the patient is in shock. It may then be given intermittently as long as circumstances dictate.

Shock is occasionally complicated by heart failure. Adequate treatment of failure will often successfully terminate the attendant shock. Failure is discussed later in this paper.

Disturbances of Rhythm

Disturbances of rhythm are common during the first few days after onset of myocardial infarction. Numerous patients have transient bouts of various arrhythmias; more uncommonly the disturbance is permanent.

Among the ventricular arrhythmias, premature beats are the most common. Tachycardia is always an ominous sign because it may lead to ventricular fibrillation and death within minutes.

Atrial premature beats, tachycardia, flutter and fibrillation all occur. The last two have, in general, a poor effect on prognosis. The danger lies not in the arrhythmias per se, but in that during the disturbance, with its rapid rate or irregular rhythm, there is decreased cardiac filling and output, decreased coronary artery flow, and increased myocardial metabolism. The last effect adds to the oxygen needs of the heart; the first two decrease the available supply.

Atrioventricular block is not uncommon. If of severe degree, it may cause further cardiac difficulty or Morgagni-Adams-Stokes attacks.

Treatment is both prophylactic and definitive. Because of dangers inherent in the ventricular arrhythmias, prophylaxis is of importance. Quinidine, 3 gr. (200 mg.) every 4 to 6 hours, or pronestyl, 250 to 500 mg. every 6 hours, are useful agents. Quinidine is also effective in preventing atrial arrhythmias. Parenteral use of these agents is dangerous and should be utilized only in treating ventricular arrhythmias. Quinidine lactate, gluconate or hydrochloride (injectable) may be given intramuscularly in doses of 0.4 to 0.6 gm. and repeated at 2 hour intervals if needed. These preparations may also be given intravenously, or a solution of 3.3 gm. dissolved in 500 cc. of normal saline or 5 per cent glucose may be given by slow intravenous drip. Because of its dangers, this drug should be given extremely slowly and, if possible, with adequate electrocardiographic control. Pronestyl hydrochloride may be administered intravenously in doses of 0.5 to 1.0 gm. at a rate not to exceed 0.1 gm. per minute. If given too rapidly hypotension may follow; this may be prevented by means of 10 mg. of Vasoxyl given with pronestyl.

In the case of the rapid atrial arrhythmias treatment must be guided by circumstances and the nature of the disturbance. Vagal stimulation by means of morphine, carotid sinus pressure, or by the use of pressor substances where shock is a complication may be sufficient. Of other medications, digitalis is the drug of choice. It should be administered cautiously and should be given intravenously only in cases of great urgency. Where one may be reasonably certain the patient has not been digitalized, lanatoside C (CEDILANID®) may be given in a single dose of 1.6 mg. (8.0 cc.) or in smaller divided doses until the desired effects or toxic symptoms appear. When the patient has previously received an insufficient amount of digitalis, either lanatoside C may be used in small divided doses or ouabain may be given as follows: 0.5 mg. of ouabain may be diluted in 20 cc. of distilled water and given intravenously at a rate of 1.0 cc. per minute. Because this agent is rapid in

action, its effect will start to become evident during administration. If no effect is observed, a second injection may be given in similar manner. Oral digitalization is usually not used in this complication because of the urgency of the condition. The desired effects are conversion of the tachycardia to normal rhythm or to an increased A.V. block, with a decrease in the ventricular rate in flutter and fibrillation.

Treatment is not needed for minor degrees of atrioventricular block. When it is so severe as to cause symptoms, however, isopropylarterenol, ephedrine, or PAREDRINE® hydrobromide is usually effective.

Thromboembolic Phenomena

Thromboembolic phenomena may originate either within or outside the heart. Thrombi which occur within the heart are usually considered in three categories: (1) There is extension of the original occlusion and infarction; many authors state that this does not happen. (2) There is the possibility of a new occlusion in some other coronary vessel with subsequent infarction. (3) Mural thrombi have been shown to occur in about 50 per cent of necropsied patients; mural thrombosis may lead to pulmonary or peripheral arterial embolism. These lesions are probably closely related, among other factors, to the increased coagulability of blood known to occur after myocardial infarction.

Extracardiac thromboembolism may be divided generally into two main groups: (1) thrombosis in cerebral arteries already diseased, especially in patients in shock or those in whom previous hypertension is replaced by hypotension, and (2) peripheral venous thrombosis with subsequent pulmonary embolism and infarction.

While the mortality due to thromboembolism has been reduced by the use of anticoagulants, indications for such therapy are not yet definite or clear-cut. Opinion ranges from the belief that every patient with myocardial infarction should receive anticoagulants to the concept that only in poor risk patients, such as those with complications, should the medications be used.

In addition to the usual medical contraindications, there is the important factor of inadequate laboratory control of the patient's prothrombin concentration. Under these circumstances the morbidity and mortality due to bleeding from anticoagulants may be greater than the mortality from thromboembolism. There is no reason, therefore, to use these agents unless adequate laboratory control is possible.

Treatment is largely prophylactic. Definitive measures used once thromboembolism has appeared are beyond the scope of this paper. Prophylaxis includes passive leg and foot exercises, prompt treatment of conditions leading to thromboembolism (such as congestive heart failure), and the use of anticoagulants.

Anticoagulants commonly used are heparin and antiprothrombin agents. Heparin ordinarily is used early, primarily to prevent thrombosis while the slower-acting, oral anticoagulant is achieving its desired effect. Heparin is available as a soluble preparation for intravenous injection, as a repository form for intramuscular injection, and as a lipid for injection into deep subcutaneous fat. The usual dose of soluble heparin is 50 to 75 mg. intravenously every 4 to 6 hours; that of the repository form is 200 to 400 mg. every 12 to 24 hours, and that of the lipid, 100 to 200 mg. every 12 to 24 hours. The proper dosage and time schedule is adjusted by means of clotting time determinations. The clotting time should be checked just before a dose is due, and the amount and frequency of administration set to keep the clotting time at 20 minutes or longer.

Because of difficulties inherent in prolonged therapy with heparin, DICUMAROL®, TROMEXAN®, or one of the more recently available phenylindanedione preparations is preferable for long-term therapy. Regardless of which product is used, however, the goal to be achieved is a prothrombin level between 20 and 40 per cent of normal. The usual procedure is to obtain a control prothrombin determination at the outset and to repeat the test daily. Suggested doses of Dicumarol to be given daily may be readily and simply determined from the following chart:

Prothrombin *(per cent)*	Dicumarol* *(milligrams)*
100-80	300
80-60	200
60-40	100
40-20	50
20- 0	0

*Tromexan dose is usually about three times that of Dicumarol.

If phenylindanedione is used, the usual initial dose is 200 to 300 mg. given in divided doses twice daily. The maintenance dose is 25 to 100 mg. daily in divided doses.

Should bleeding occur following the use of heparin, withdrawal of the drug will usually suffice. With the other agents, however, in addition to withdrawal, vitamin K_1 (MEPHYTON®, Merck) may be given intravenously in doses of 50 mg. or more as indicated. In most patients the prothrombin percentage will return to normal ranges within a relatively short time. Transfusion with *fresh* whole blood or plasma is also indicated.

Anticoagulants should be administered for 6 to 10 weeks or longer as each individual case dictates.

Acute Left Ventricular Failure

Acute left ventricular failure occurs as a rule at the onset or within the first few days. The symptoms of dyspnea, orthopnea, cough and a sense of suffocation, and the signs of cyanosis, rales at the lung bases, diaphoresis, accentuated P_2, gallop rhythm, and tachycardia are no different from those of acute left ventricular failure associated with other forms of heart disease. Untreated, the condition may go on to acute pulmonary edema.

Treatment is aimed at decreasing extracellular fluid volume and supporting the weakened myocardium. The usual measures employed are digitalis, a low sodium diet (rigid restriction should be avoided in the presence of renal failure), mercurial diuretics, oxygen, venesection or bloodless phlebotomy, a sitting position in bed or in a chair, and, of great importance in acute pulmonary edema, morphine sulfate in doses sufficient to achieve a desired effect without causing respiratory embarrassment. Most of these measures need not be discussed here.

The rate of digitalization must be determined by the individual needs of each patient. Intravenous digitalization has been discussed above. Of oral preparations, we prefer gitalin (GITALIGIN®, White) because it acts rapidly, is quickly excreted, and has a wide range between therapeutic effect and toxic dose. A convenient method for establishing the required dosage is to give 0.5 mg. per 10 pounds of body weight. If the total estimated dose is thus calculated, half may be given immediately and the remainder in divided doses every 2 hours until therapeutic or toxic effects appear. When the therapeutic effect is achieved, the patient may be placed on a maintenance dose of 0.5 mg. or more per day as needed. If toxicity develops, the drug should be withheld until it disappears, and then the maintenance dose should be given. It is unlikely that carefully followed patients will be made toxic with gitalin. If a slower method is desired, the dosage is calculated in the same manner but administered in smaller amounts over a longer period of time. For example, if the total calculated dose is 7.5 mg., the patient may be given 1.5 mg. every 4 hours for 5 doses. Or, more slowly still, he may be given 1.0 mg. 3 times daily for 3 days. The increased total dose (9.0 mg. instead of 7.5 mg.) on this schedule allows an increment to replace the estimated daily excretion of 0.5 mg. Similar schedules may be established for digitalis leaf. Here the total dose is calculated on the basis of 0.1 gm. per 10 pounds of body weight.

If DIGITOXIN® is used, either 1.2 mg. may be given as a single dose or 0.6 mg. may be given immediately and followed with 0.2 mg. every 2 hours until saturation is reached. DIGOXIN® 2.0 mg. immediately and 0.25 mg. every 2 hours until the patient is saturated is another preparation and method which may be used. Digitoxin and Digoxin may also be given by the slow multiple dose method. In any case, maintenance doses must follow initial digitalization. These must be determined individually.

These methods assume that the patient has not previously received digitalis. If he has, and the interval since his last dose is known,

an estimate may be made of his deficiency, and he may then receive the needed amount cautiously in divided doses. If the interval is unknown, even more care must be used, but the drug should not be withheld.

Use of a low sodium diet in a patient with normal kidneys may prevent the appearance of congestive heart failure. Such diets may be obtained in suitable texts or from hospital dieticians. A convenient formula suitable for use during the first few days after infarction consists of:

Lonalac	250 gm.
Protenum	100 gm.
Cane sugar	125 gm.
Distilled water to make a total of 2000 cc. of formula.	

Eight ounces each hour (an ordinary drinking glass) will give sufficient calories and fluid. Supplementary vitamins should be given.

Any accepted mercurial diuretic should be used where indicated in ordinary doses.

Right ventricular failure may appear at any time within the first few weeks, especially if the patient has been in shock. Diagnosis and treatment are the same as in congestive failure from any cause.

Complications Causing Death

Rupture and perforation of the ventricular wall, interventricular septum and the papillary muscle are probably the most dramatic fatal complications of myocardial infarction. These complications usually appear within the first three weeks after infarction; more rarely they may occur at a later date. Rupture of the ventricular wall occurs in 8 to 10 per cent of all patients who die of myocardial infarction. In a group of 80 such fatal cases we have studied, the complication was found uniformly to appear in patients over the age of 50, more commonly in women than in men, hypertensives whose blood pressure remained elevated after infarction, and those who had, as a rule, transmural infarction. No definite correlation was found between perforation and moderate degrees of physical activity. The cause of death in these patients is hemopericardium with cardiac tamponade; the complication is uniformly fatal.

Interventricular septal perforation probably occurs in less than 5 per cent of patients who die of myocardial infarction. The diagnosis is easily made; a thrill and murmur similar to that found in interventricular septal defect appears in a patient where it has not been present previously. Cardiac failure ensues rapidly; the longest survival on record is a patient who lived five years after perforation. Papillary muscle rupture for any reason is an extremely rare complication, and less than 50 such patients have been reported. This lesion can be diagnosed by the sudden appearance of a coarse, loud, apical systolic murmur and the rapid onset of congestive heart failure. Treatment of ventricular wall rupture is without avail; that of interventricular septum and papillary muscle rupture consists of treatment of the subsequent congestive heart failure.

Other Complications

Ventricular aneurysms appear in about 10 per cent of patients. They are thought to form at sites of mural thrombosis or where the ventricular wall is thinned and weakened, especially in patients who have been in shock or failure or have been made ambulatory too soon. It is important to recall that during periods of shock or congestive failure, coronary blood flow is decreased—is inadequate—and there may be ballooning of the ventricular wall in the region of infarction. This may be responsible for the development of the aneurysm. Treatment is prophylactic and consists of prevention of those complications associated with aneurysm.

Myocardial calcification may occur in the scarred area in a small number of patients. By itself, this condition is usually of little consequence as concerns function of the heart.

Pericarditis is a complication which frequently appears in myocardial infarction, but is never serious except for a few rare reported instances of hemopericarditis subsequent, probably, to anticoagulant therapy.

Periarthritis of the shoulder appears in about 15 per cent of patients, and the *shoulder-hand syndrome* in about 5 per cent. Of these patients, 20 to 25 per cent develop irreparable trophic changes of the skin, tendons, muscles,

fascia and bones. The complication usually appears 3 to 12 weeks after infarction and the pain and disability may last a year or more. Treatment is generally unsatisfactory and is usually best handled by means of adequate physiotherapy and supportive measures.

Permanent reduction of cardiac reserve may occur after infarction. This may take the form of angina pectoris, coronary insufficiency or chronic congestive heart failure. Recognition and management of these conditions do not differ from those in ordinary circumstances.

Finally, *cardiac neurosis* frequently appears after myocardial infarction. It may be wise to recall that of those suffering myocardial infarction, about 80 per cent recover from the first attack. Of these, about half will probably return to a full-time gainful occupation. At present, the average duration from the onset of angina pectoris or infarction to death is about 8 to 10 years. These patients, therefore, should be reassured, and everything possible should be done by the physician to see that they are not left hopeless neurotic cripples.

Treatment of Peripheral Vascular Diseases

II. DISEASES OF THE VEINS OF THE LOWER EXTREMITY

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Varicose Veins

PROBABLY the most common surgical disease afflicting the human race is varicose veins. They develop, it is believed, because of a congenital defect in the valves of the deep veins and in the proximal ends of the saphenous veins. They are frequently hereditary since it is not uncommon to find them in the children of parents who have them. The most common symptom is pain, especially after standing for long periods. In women, their unsightly cosmetic appearance frequently brings the patient to a doctor for treatment. They also may be the cause of chronic dermatitis or ulceration of the lower extremity, but they rarely produce lymphedema of a severe degree. Both the long, or internal, saphenous vein and the short, or external, saphenous vein are usually involved along with their numerous tributaries.

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The treatment of varicose veins has gone through many cycles. It is of interest that from 1840 to 1845, many patients were admitted to the Massachusetts General Hospital in Boston for an injection treatment with a solution of ferric chloride. Undoubtedly the complications of this form of treatment before the days of asepsis caused it to be discontinued. This method was rediscovered, so to speak, in the 1920's using a different sclerosing solution, but at the present time it has again been discarded because of unsatisfactory results. Not only do the veins recur after the injection therapy but, in some instances, the condition of the leg is made much worse due to the fact that the sclerosing solution used to inject the veins may spread to involve other veins, such as the communicating or deep veins, and when they canalize, the condition of the leg becomes more serious because the valves of these veins have been destroyed.

At the present time it is believed that the

best method of treatment is the radical removal of the main trunk of the long and short saphenous veins. The operation should be done under a general anesthesia and after ligating it at the saphenofemoral junction, every effort should be made to remove the main trunk of the long saphenous vein from the groin to below the internal malleolus by a subcutaneous stripping procedure. A similar procedure should be performed to remove the short saphenous vein from the popliteal space to the level of the external malleolus. Ambulation within 24 hours after the operation is imperative to prevent thromboembolism. Following the removal of these veins, small injections of a sclerosing solution are used to obliterate the tributaries not removed by the stripping procedure. If a patient is 60 to 65 years of age or older, it is believed best not to use this radical procedure because of the danger of thromboembolism, unless a stasis dermatitis or a chronic ulcer is present. Under these conditions it is believed justifiable to resort to this radical treatment. If these complications are not present in the elderly patient, some form of elastic support, preferably an elastic stocking or an elastic bandage, is the treatment of choice.

Venous Thrombosis or Phlebitis of the Lower Extremity

Superficial venous thrombosis—Thrombosis developing in large, tortuous varicose veins is a fairly common complication of this condition. The diagnosis is readily made because of a tender, firm, hard, cordlike clot within the dilated vein. The treatment recommended for this condition is to perform a high interruption of the saphenous vein at the saphenofemoral junction and, through multiple small transverse incisions, to excise the large thrombosed vein. The purpose of this treatment is to prevent a propagation of the clot in the saphenous vein from extending into the deep venous circulation from which a pulmonary embolus could arise. In some instances it also may be helpful to strip the main saphenous trunk from the groin to just below the knee. If this surgical procedure is performed, it is imperative that the patient be ambulatory within 24 hours after the operation to prevent deep venous thrombosis from occurring.

Deep venous thrombosis—This is a serious condition which occurs most frequently following major surgery, pregnancy or trauma to the extremity; in some instances it may even occur spontaneously. There are two schools of thought in regard to the treatment of this condition. One advocates a medical treatment with anticoagulants and the other recommends surgery, consisting of interrupting the deep venous system in the groin. It is believed the latter method is preferable, providing the venous thrombosis is seen early. It is recommended under these conditions that the femoral vein be interrupted distal to the saphenous vein and, in most cases, distal to the bifurcation of the common femoral vein. The superficial femoral vein—unless it contains a clot—is interrupted just distal to the profunda femoris vein. If a clot is found in it or in the common femoral vein, it should be removed by aspiration and the common femoral vein ligated and divided *proximal to the profunda femoris branch but distal to the saphenofemoral junction.*

If the anticoagulant method of treatment is to be followed, it is recommended that the patient be started on 600 to 900 mg. of tromexan by mouth and at the same time 200 to 300 mg. of DICUMAROL®. The former drug takes effect much more quickly than the latter, but once the prothrombin time has been prolonged by the tromexan, the treatment can be continued with Dicumarol which is much cheaper and just as effective. It is imperative, if this method of treatment is carried out, that a reliable laboratory should be available where daily prothrombin time determinations can be made; otherwise under no circumstance should the anticoagulant therapy be used. Unfortunately, in our hands, the anticoagulant therapy has not been too effective since pulmonary embolism frequently occurs with this form of therapy, probably because of the difficulty in reducing the prothrombin activity to prevent further thrombus formation.

At present it is believed that if a patient has had a minor pulmonary embolus, irre-

spective of whether the extremities show any signs of deep venous thrombosis or not, both femoral veins should be interrupted, and, in addition, the patient should be placed on anticoagulant therapy. Interruption of the inferior vena cava is reserved chiefly for (1) those patients with pulmonary emboli arising from a pelvic thrombophlebitis associated with a septic process in the pelvis and (2) those patients who continue to have pulmonary emboli after femoral vein interruption and adequate anticoagulant therapy.

Ulcerations of the Lower Extremity

Chronic ulcerations of the lower leg may occur because of simple varicose veins, or they may develop secondary to the postphlebitic syndrome due to interference with circulation in the superficial, deep and communicating veins of the lower extremity. The treatment of the first type of ulceration is relatively simple. It is first healed by means of tight elastic adhesive bandages wrapped around the leg over gauze bandages. When healing has been accomplished, a permanent cure is obtained in most instances by a radical removal of the long and short saphenous veins by the stripping procedure. In addition one will usually find an incompetent communicating vein near the ulcer which can be isolated, ligated and divided through a small separate incision in the lower leg.

The problem of postphlebitic or post-thrombotic ulcerations is far different because they are much more difficult to heal, but this can also be accomplished by the elastic adhesive type of bandage applied to the lower leg over a gauze bandage. After the ulcer is healed a cure can be obtained in the majority of cases by a radical removal of the long and short saphenous veins, a ligation of the communicating veins on the inner side of the lower leg, and an interrruption of the diseased superficial femoral vein distal to the profunda femoris branch in the groin. It is essential that all sepsis be eradicated before performing this type of surgery. Following the operation it is necessary that the patient continue to wear an elastic support on the lower extremity for an indefinite period of time because lymphedema is present in all post-thrombotic extremities, and if it is not controlled the results are not satisfactory. A heavy weight, two-way stretch type of elastic stocking with a heel is the best method of controlling this edema.

There is one other type of chronic ulceration of the lower extremity that must not be confused with the varicose and post-thrombotic type, namely, the arteriosclerotic ulceration. This usually can be diagnosed by careful evaluation of the arterial circulation of the extremity, and if arterial pulses are absent, one must be very careful not to embark on the extensive surgical procedure described above. This type of lesion is usually best treated by antibiotics, lumbar sympathectomy and, in some cases, restoration of the arterial continuity by arterial or venous grafts.

Lymphedema of the Lower Extremity

Chronic lymphedema of the lower extremity is a common complication following deep venous thrombosis and is best treated by using the heavy weight type of elastic stocking described above. There are many other patients, especially young women, who have an idiopathic type of lymphedema which develops for no known cause. It should be pointed out that if the edema is not controlled in these patients by the proper type of elastic support, the condition will grow worse and finally develop into a typical case of elephantiasis. It is believed that if the proper elastic support is worn early in the course of the disease—and this should be a heavy weight type of elastic stocking with a two-way stretch—the edema can be controlled and the serious complications of elephantiasis can be averted. In addition, in most instances, if the case is seen early in the course of the disease it will be possible to return the leg to a normal size. Lumbar sympathectomy should not be performed for either the postphlebitic type of ulceration or chronic edema of the lower extremities because in many cases it makes the condition worse and rarely improves it.

Pediatrics IN GENERAL PRACTICE

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The Treatment of Acute Bacterial Meningitis in Infants and Children

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THE prognosis for patients with bacterial meningitis has improved greatly in the past decade and a half since the widespread use of type-specific antiserums and various chemotherapeutic and antibiotic agents. Nevertheless far too many people still die each year of meningitis. The actual mortality rate is impossible to ascertain, but the official mortality figures for so-called "cerebrospinal meningitis" in the United States since 1945 lie in the vicinity of 25 per cent.[1] This figure may seem startling to those who work in university medical centers, but one must remember that most patients with meningitis are not treated in university medical centers but in general hospitals, many of them in rural areas. Most of the deaths from meningitis occur in children. In analyzing the reasons for these deaths Alexander,[2] in 1945, classified them as follows: (1) failure of early clinical diagnosis; (2) inadequate laboratory facilities for accurate and rapid identification of the etiologic agent; (3) improper selection and use of therapeutic agents. As she points out again in 1953, these 3 factors still account for most of the deaths from meningitis. Our experience is in complete accord. Since laboratory facilities will probably always be suboptimal in all but a few hospitals, a realistic approach to reducing further the mortality from meningitis must by-pass the need for certain laboratory procedures and for delicate judgment in choice and administration of drugs.

The study here reported was designed in the autumn of 1950 to evaluate the results obtained when all patients with "purulent meningitis" were treated according to the same regimen, regardless of causative organism. Careful bacteriologic studies were carried out in each case, so that it would be possible in retrospect to evaluate the treatment in each type of meningitis. Eighty-six consecu-

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tive patients were so treated; the information obtained suggests that it is possible to treat patients suffering from acute pyogenic meningitis according to a rather standard regimen and to obtain reasonably good results.

Outline of Study

The study was carried out over a period of 2 years, from January 1951 to January 1953. During that time 98 patients with meningitis were admitted to the Contagious Disease Service of the Tulane Pediatric Department at Charity Hospital. Of that number 86 are included in the present analysis.

In reviewing the data it was found necessary to eliminate from consideration the following 8 patients: 2 children, each aged 2 years, with meningococcal meningitis; a 2 year old child with meningitis due to *Hemophilus influenzae;* 4 infants less than 1 year of age in whom the etiologic agent was not identified, and a 3 months old infant with pneumococcic meningitis. All 8 of these patients recovered, but cannot be considered here because through error the planned therapeutic regimen was not followed. Two newborns with *Escherichia coli* meningitis were intentionally treated with other antibiotics. One 4 month old infant died within 15 minutes of admission to the hospital, before adequate therapy could be instituted. One patient was transferred from another hospital where for many weeks he had received inadequate treatment for *H. influenzae* meningitis and was suffering from hydrocephalus when he was admitted to this hospital.

With the exceptions listed above, the 86 patients reviewed here represent a consecutive series of admissions for acute bacterial meningitis.

Treatment

The routine of treatment was as follows: Each patient was examined on admission. A lumbar puncture was performed and the pressure was determined; spinal fluid was obtained in the usual fashion for smear, culture, cell count and chemical analysis. The patient was then immediately given intravenous sodium sulfadiazine (50 mg. per kilogram of body weight), also aqueous penicillin (200,000 units intravenously, regardless of age or weight). At the same time sulfadiazine was given by mouth or by stomach tube (100 mg. per kilogram of body weight), also chloramphenicol (100 mg. per kilogram of body weight). Subsequent medication consisted of sulfadiazine (150 mg. per kilogram of body weight daily, divided into 4 or 6 doses); chloramphenicol (250 mg. every 6 or 8 hours, depending on the size of the child), and aqueous penicillin (200,000 units intramuscularly every 8 hours). It should be emphasized that, in the case of sulfadiazine, both initial and follow-up doses were calculated on the basis of the child's weight; in the case of chloramphenicol the initial dose was so calculated, but the follow-up dose was estimated in a rather crude fashion. For penicillin the child's weight was not taken into account at all.

Treatment was continued for a minimum period of 6 days or until the patient had been afebrile for 48 hours, whichever was longer.

Follow-up lumbar punctures were performed on the second and fifth hospital days, subsequently only on special indication.

Bacteriologic Data

H. influenzae was demonstrated by culture, or by smear and direct "quelling," from 32 patients, *Neisseria meningitidis* (meningococcus) from 26, *Diplococcus pneumoniae* (pneumococcus) from 14. From 14 additional patients no organism could be recovered; of these, 4 showed *H. influenzae* in cultures from the throat or nasopharynx, and one a pure culture of pneumococci.

All cases of *H. influenzae* meningitis were due to type B. From the patients with pneumococcal meningitis the following types were recovered: VI (3 cases); XIV (2 cases); XIX (2 cases); XXIII (2 cases); III, VII, XVIII, XXIX (1 case each). In one case the pneumococcus was not typed.

Of the 57 patients whose admission spinal fluid cultures were positive on more than one occasion, all were suffering from *H. influenzae* meningitis; they will be discussed in more detail.

Clinical Data

Seasonal incidence—The findings on the 86 patients are plotted in Figure 1 according to month of admission and etiologic agent. Despite the fact that this study was carried out in a subtropical area, the preponderance of *H. influenzae* meningitis in the late autumn months and the peak incidence of meningococcal meningitis in the late winter and spring is in agreement with the observations from other parts of the country.[3,4]

Age—As shown in Figure 2, 51 out of a total of 86 patients were less than 2 years old; i.e., more than half of the patients fall into the age group where the mortality is likely to be highest.[4a,5]

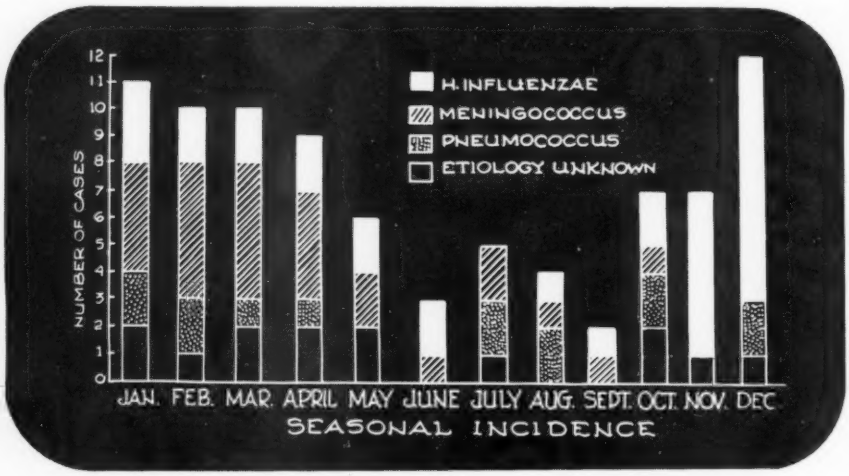

FIGURE 1. Monthly incidence of different types of bacterial meningitis in 86 patients under the age of 10 years.

Treatment prior to admission—Sixty-two patients gave a definite or probable history of treatment with antibiotics or sulfanomides prior to admission. Of this number only 11 yielded no organism on culture of the spinal fluid.

Mortality

The mortality is shown graphically in Figure 3. Three patients with *H. influenzae* meningitis died 6 hours, 30 hours and 48 hours, respectively, after admission. Three patients with pneumococcal meningitis died 2 hours, 7 hours and 4½ days, respectively, from the time of admission. One patient with meningitis of unknown etiology died within 6 hours.

Complications

Subdural effusion and empyema—Subdural taps were performed when indicated. Six of the 14 patients with pneumococcal meningitis developed subdural effusions,[6] all sterile on culture.

Four patients with *H. influenzae* meningitis developed sterile effusions. Another patient, a 7 month old infant, was found 12 days after admission to have a subdural empyema which yielded *H. influenzae* on culture. A fifth patient in this group, also 7 months old, was found to have a subdural empyema at the time of admission; she died 2 days later.

One patient with meningitis of unknown etiology developed a sterile effusion.

Late sequelae—Two patients with *H. influenzae* meningitis showed evidence of severe cerebral damage at the time of discharge. The other patients were not obviously damaged. Careful follow-up studies unfortunately have not been possible.

Drug reactions—None were observed.

Chloramphenicol Palmitate in H. influenzae Meningitis

The original outline of treatment did not

specify whether patients were to receive powdered crystalline chloramphenicol or the palmitate ester of chloramphenicol.[7] As a result 14 patients received chloramphenicol palmitate, 6 of them patients with *H. influenzae* meningitis, aged respectively 3 months, 7 months, 8 months (3 cases) and 24 months. Of the 6, one died; 1 showed a positive spinal fluid culture 12 days after admission, also subdural empyema; 2 had positive spinal fluid cultures on the day after admission and developed sterile effusions later; 1 had a positive spinal fluid culture on the second hospital day but recovered uneventfully; 1 went home with evidence of severe brain damage.

Of the 26 patients with *H. influenzae* meningitis who did not receive chloramphenicol palmitate, 2 died, 2 developed late sterile subdural effusions, and 22 recovered uneventfully. None yielded a positive spinal fluid culture after the initial spinal tap.

These data suggest that chloramphenicol palmitate should not be relied on in the treatment of any patient who is or may be suffering from *H. influenzae* meningitis. The reason is probably to be sought in the delayed absorption and lower blood levels of chloramphenicol obtained when the drug is given in the form of palmitate, as shown by Ross, Burke and Rice,[8] and by Yow and associates.[9]

Discussion

The combination of drugs selected here was chosen as presumably effective against the 3 bacterial species which most commonly cause meningitis in children: *H. influenzae*, pneumococcus, meningococcus.

Sulfadiazine was included because accumulated experience has proved its excellence in the treatment of meningococcal infections, and because it is likewise effective against *H. influenzae* and the pneumococcus.[10] Wherever possible, we recommend giving the initial dose intravenously, to avoid any delay in reaching effective blood levels. If, however, the intravenous route is impractical, the initial dose of sodium sulfadiazine may be given subcutaneously as a 1 per cent solution in physiologic saline (100 mg. per kilogram of body weight). A 5 per cent solution in saline or in glucose may be used as an alternative if necessary.

Chloramphenicol is still, in our experience, the drug of choice in *H. influenzae* meningitis. AUREOMYCIN® and TERRAMYCIN® are without doubt both effective, but they are less rapidly absorbed into the blood and spinal fluid than chloramphenicol,[11] which is a great drawback when dealing with a serious infection in children. The delay in absorption probably ac-

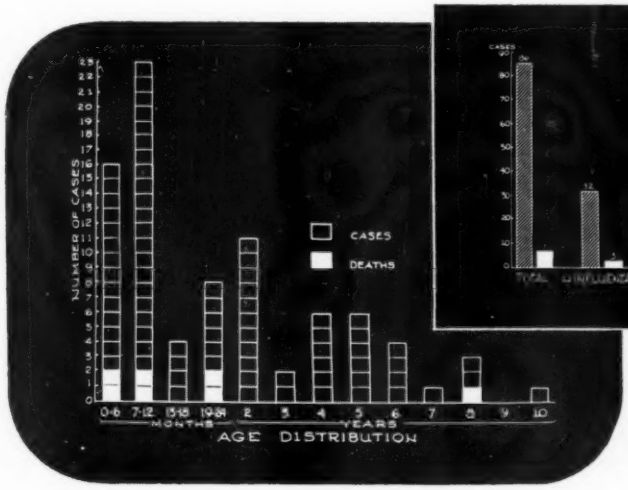

FIGURE 2. Age distribution of 86 patients with bacterial meningitis.

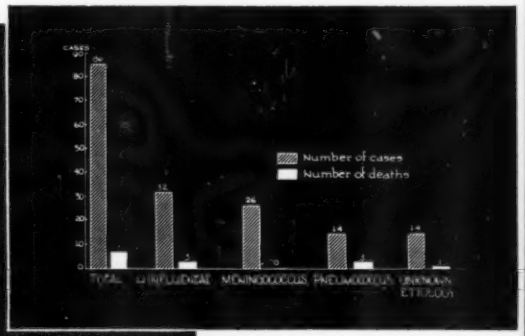

FIGURE 3. Mortality according to etiologic agent in 86 cases of bacterial meningitis.

counts for the persistence, in some cases, of positive spinal fluid cultures for several days after the start of treatment.[12] With the exception of the patients treated with chloramphenicol palmitate, as mentioned before, the results in our cases of *H. influenzae* meningitis compare favorably with those of recent series from other clinics where different regimens were followed.[10, 13]

The death of 3 of the 14 patients with pneumococcal meningitis (22 per cent) raises the question as to the results obtained with other methods of treatment in this disease in infants and children. Nemir and Israel[14] reviewed the recent literature on infants and children treated for pneumococcal meningitis and found the mortality rate to be 19 per cent; they found no significant difference between the patients treated with intrathecal penicillin and those where intrathecal medication was omitted. The series of Dowling and his co-workers,[15] where massive doses of systemic penicillin were used in treatment of pneumococcal meningitis (with exclusion of all other agents) includes only 5 children, 3 of whom died; the overall mortality in their 21 patients was 38 per cent. Lowrey and Quilligan,[16] treating infants and children with systemic penicillin in combination with sulfadiazine, had 3 deaths among 18 patients (17 per cent mortality). The evidence summed up here suggests that neither intrathecal administration of penicillin nor massive dosage as recommended by Dowling and his co-workers contributes to lowering the mortality in this disease.

What about antagonism between chloramphenicol and penicillin? Despite laboratory evidence for the existence of such antagonism under certain very sharply defined experimental conditions,[17] only Lepper and Dowling[18] claim to have found clinical evidence of such antagonism: In their group of 43 patients with pneumococcal meningitis treated with massive doses of systemic penicillin, 13 (30 per cent) died; among 14 patients treated with both Aureomycin and penicillin, 11 (79 per cent) died. If one examines only the data pertaining to children under the age of 13 years, 3 of the 11 patients treated with penicillin alone died, but neither of the 2 patients treated with both Aureomycin and penicillin! Furthermore it can readily be seen that even their "better" group, i.e., those treated with penicillin alone, showed a 30 per cent death rate, compared with 22 per cent in our group. Thus it appears that, insofar as one can judge from so small a number of patients, our results in pneumococcal meningitis are in line with those from other clinics.

The schedule of drug administration should next come under scrutiny. It should be noted that in our patients none of the 3 drugs was administered more often than every 6 or 8 hours. Accumulating evidence, ably discussed and summarized,[19] suggests that larger doses of antibiotics, given less frequently, are just as effective in combating infection as smaller ones given more often. Less frequent drug administration is vastly preferably for the patient, since rest is vital; it also lightens the tasks of the nursing personnel. The drugs which we have employed might also be given by other routes: subcutaneous sulfadiazine, intramuscular chloramphenicol, etc. We cannot recommend them wholeheartedly simply because we ourselves have not had sufficient experience in their use.

Recommended Treatment

Based on the considerations discussed and on the experience gained during this 2 year study, the accompanying outline of treatment is proposed (Table 1). It should be emphasized that this form of treatment, using several antibiotics, is not advocated as an ideal one for the use of teaching centers where accurate bacteriologic studies are available. We do not approve of using antibiotics or sulfonamides needlessly, thereby running the risk of sensitization reactions, unpleasant side effects, and so forth. Nor is this type of treatment suitable for premature and newborn infants with meningitis, since the etiologic agent of meningitis at this age is in most instances one of the enteric bacteria[20] where polymyxin or streptomycin may be the drug of choice.

Summary

1. Eighty-six consecutive patients under the age of 10 years with acute purulent meningitis

TABLE 1

TREATMENT FOR PURULENT MENINGITIS
(Patient more than 2 months old)

	DOSE	
	Initial	*Continuing*
Aqueous penicillin	500,000 U., I.V.	500,000 U., q. 8 h., I.M.
Sodium sulfadiazine	50 mg/kg., I.V. (5% solution, 1 cc./lb.) 100 mg./kg., P.O.	50 mg./kg. q. 8 h., P.O.
Chloramphenicol *(not palmitate)*	100 mg./kg., P.O.	250 mg. q. 8 h., P.O.

Discontinue treatment after 7 days or when temperature has remained normal for 2 days.

were treated according to a combined regimen of sulfadiazine, chloramphenicol and penicillin; the mortality rate was 8.1 per cent.

2. Bacteriologic studies showed that in 32 patients *H. influenzae* was the etiologic agent, in 26 the meningococcus; in 14 the pneumococcus. In 14 the etiologic agent could not be identified.

3. Analysis of the data suggests that, where reliable bacteriologic help is not available, the above 3 drugs in combination may be used in the treatment of any child, more than 2 to 3 months of age, with purulent meningitis with expectation of a satisfactory outcome.

4. An unusually high incidence of complications in patients with *H. influenzae* meningitis who were treated with the palmitate ester of chloramphenicol suggests that this compound is to be avoided in children who have severe, acute infections.

The authors are indebted to Dr. G. J. Buddingh, Professor of Microbiology at the Louisiana State University School of Medicine, for many bacteriologic studies on patients.

The chloramphenicol and the chloramphenicol palmitate used in the early part of this investigation were kindly supplied by Dr. H. E. Carnes, of Parke, Davis and Company.

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Pediatric Responsibility to Children with Speech Defects

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ADVICE concerning the care of children whose speech is defective should be generally available to parents through their pediatrician or their family physician. Unfortunately, family physician and pediatrician alike have been prone to rely on the comforting but often erroneous prediction, "Let him go; he'll outgrow it." A large number of children do not "outgrow" their speech defects, and by the time they have been brought to the speech therapist, precious years have been lost, and irreparable damage may have been done. The informed physician can render invaluable assistance to these children in the prevention or treatment of their individual speech problems.

One of the distressing things about speech defects—severe or mild—is that the child, his parents, his teachers and his playmates cannot help but evaluate the abnormal speech. Such evaluation is almost inevitably on the side of a personal derogation by which the child is penalized. He is more than likely to develop a low estimate of his personal worth, sometimes to the extent that his initiative is virtually paralyzed. Socially he will have fewer opportunities for acceptance than the child with normal speech. His educational achievements are likely to be hampered by his feelings of inferiority and his difficulty in class recitations. Many a speech-handicapped child has left school before his education was completed merely because he could not face the embarrassment and the social competition of school. Favorable employment and even military service are frequently denied the person who cannot communicate normally. Since several million people in the United States have handicapping speech defects, the total effect is thus not only one of depreciated personal values, but also of general loss to society.

The incidence of speech disorders among children cannot be estimated with accuracy for all parts of the country. Local conditions of health, economy and culture have much to do with the frequency of occurrence and the nature of the speech defects in any particular community. A survey reported by the Tennessee Department of Public Health[1] records a local incidence of 9.4 per cent of children with defective speech, of whom 1.6 per cent were found to have major speech defects. The report indicates a gradual decrease in the number of speech defects until about 9 years of age, after which the incidence remains fairly stable. Whereas reports of other surveys vary considerably from these figures, it is a safe estimate that 5 per cent to 10 per cent of all children of school age have some form of speech abnormality.

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Prediction as to the outcome of speech defects is difficult at best. Some speech defects are relatively mild and are soon overcome by the child in the normal course of growing and learning; other defects are persistent and will continue throughout the lifetime of the person unless adequate diagnosis and therapy are provided. A small percentage are of so serious a nature that even a good program of care cannot eliminate the defect but can usually bring about valuable improvement in speech.

Since it is often impossible to decide which speech defects will improve spontaneously and which ones can be improved only by therapy, it should be our business to render all possible help wherever speech defects exist. The acids of self-depreciation should not be allowed to etch indelibly the personalities of these children as long as the means exist to prevent or correct the defects.

A comprehensive program for the treatment of children afflicted in speech may involve a number of specialists and diagnostic and treatment agencies. Inasmuch as parents often turn first to their pediatrician, it is important that he be in a position to render at least three basic services to the child whose speech is defective: (1) early recognition of abnormal speech development; (2) discovery and elimination or amelioration of physical and environmental conditions responsible for causing or maintaining the speech defects, and (3) referral to special clinical or educational facilities for the direct handling of the speech defect or those aspects of personality and environment closely related to it.

Classifications of Speech Defects

Recognition of the disorders of speech during the early and labile stages of a child's development is basic to a program of prevention and proper care. Speech which differs markedly from the average speech of persons of the same age, sex and cultural environment is considered defective if the voice, articulation, rhythm or language are not adequate to communicate the personal and social needs of the individual. Such speech defects usually arise from multiple, interacting causes rather than from a single cause, and the resulting symptoms often occur in a pattern of behavioral maladaptations. It is, therefore, useful to think of speech defects as syndromes, not to be diagnosed merely by an inspection of the oral cavity nor to be treated merely by attacking the speech symptoms.

There are several systems of classification in vogue with speech pathologists. The following brief descriptions of the major types of speech disorders and their etiologies are given as being sufficiently general to aid an examiner in identifying the common abnormalities.

Articulatory disorders—This term refers to disorders in which the intelligibility of speech is affected by the habitual distortions, omissions, substitutions or additions of consonants and vowels. "Dyslalia" is generally used to refer to those disorders of functional control of the tongue, lips and palate for which there is no clearly discernible neural pathology. "Dysarthria" commonly designates the articulatory defects due to lesions of the central nervous system. The speech symptoms of both types are occasionally somewhat similar, but the treatment methods may differ widely. The etiology of articulatory disorders is to be sought in physical, personality and environmental influences, but it is often complex and occasionally must be considered idiopathic. Direct speech therapy is often required. Prognosis in dyslalia is generally good if a program of care is started soon enough and if it is sufficiently comprehensive. Dysarthria is more difficult to treat, and improvement rather than elimination of the defect is likely to be the realistic goal.

Stuttering includes various forms of repetition, prolongation and blocking or the devices by which the person seeks to hide his stuttering. The etiology is believed to be mostly of a "functional" nature but may be organic in some cases. Since current theory indicates that it is at least partially a manifestation of anxiety, treatment often involves measures designed to diminish anxiety. In many cases direct speech help is needed. Prognosis should be based on an appraisal of many factors; it is often good in childhood and becomes less favorable if stuttering persists to adolescence.

Voice disorders are those in which quality, loudness, pitch or melody of voice are found to be inappropriate to the age and sex of the person. These disorders are probably more frequently overlooked than any other speech handicap. The etiology may be functional or organic. There is frequently a relationship between the characteristics of voice and personality. Voice problems in children are difficult to treat by educational methods, and prognosis is usually uncertain unless speech therapy can be combined with personality adjustment and the physical correction of vocal pathologies.

Delayed speech is a term primarily descriptive of retardation in linguistic development, and is applied to children of three or more years of age who have not yet developed language comparable to the average child of that age. The etiology may involve either organic or functional aspects, but often appears to be idiopathic. Mental retardation and hearing loss must always be suspected until ruled out. Prognosis is usually guarded.

The term "childhood aphasia" is sometimes used for those children in whom there is clear evidence of brain injury which may involve association areas of the cortex, but since the diagnostic picture is often confused in these children, it is probably best to avoid general use of the term until the syndrome has been better defined.

Aphasia (dysphasia) refers to the loss or impairment of various modalities of language because of damage to areas of the brain. The total personality may be involved. It is more common in adults than in children, but is common enough in children to warrant its consideration. Whether caused by tumor, cerebrovascular accident or cranial trauma, treatment must be intensive and comprehensive through a long-term program if practical recovery is to be achieved. Prognosis may be good if educational treatment is instituted as soon as possible and if the damage has not been too extensive.

In addition to the foregoing terms which classify speech characteristics, there are physical abnormalities which so directly affect speech that the terms diagnostic of the physical condition are also used with reference to the speech characteristics which typically accompany them.

Cleft palate speech—Congenital clefts of the lip or palate, pre- or postoperative, often affect the articulation of speech and the voice quality. The speech symptoms usually derive from complex causes, since anatomic defects of congenital origin, dental malocclusion, hearing loss and personality influences combine to play a large part in shaping the speech of the children with cleft lip and palate. Prognosis can be hopeful if a long-term program of surgery, dental care, speech therapy and personal-social hygiene is planned for and begun at the proper times. The program of total care should extend well into adult life.

Cerebral palsy speech usually includes various forms of voice disorder, articulatory disturbance, language retardation, and (not infrequently) stuttering. Although the primary defect may be neurologic, many factors of nurture and growth determine the speech characteristics of the child. Prognosis should thus depend on a multiplicity of things, but the values of early planning and long-time therapy have been repeatedly demonstrated.

Deaf speech and hard-of-hearing speech are often characterized by articulatory defects, language delay, and typical aberrations of voice. The decisions as to planning must be made with reference to the age of the child, amount of hearing loss, intelligence, social maturity, the family situation, etc. Excellent day school and residential programs are available. The prognosis for eventual satisfactory use of speech always must be made on an individual basis, but it is best where speech training, acoustic amplification and adequate educational facilities can be made available as soon as possible after the diagnosis of deafness.

Prevention and General Care

The causes of speech disorders are to be sought in the genetic record of the child, in the conditions of his birth and early development, and in the physical, environmental and personality factors which condition the first five or six years of his life. Since most

speech disorders appear in the early developmental years, it follows that their prevention, elimination or amelioration should be effected early in child life. With proper physical care and adequate environmental control, at least 75 per cent of the speech problems which plague adult life could be prevented before a child reaches puberty.

In a program of prevention, the physical and emotional events of the first year of life are most important. At the University of Michigan Speech Clinic where many hundreds of children with speech defects have been examined during the past 15 years, our histories of children with serious speech defects all too frequently reveal the occurrence of cyanosis, jaundice, rickets, early and prolonged feeding problems, virus diseases provocative of high fevers, and signs of abnormal restlessness or persistent apathy during the first year. Indications of an unstable environment, inadequate mother-child relationships, sibling problems and other evidences of potentially traumatic environmental conditions also occur frequently. Congenital anomalies of the oral, nasal or throat regions which seriously interfere with normal speech development are rare except for cleft lip and palate.

Since the average child does not talk until he is one year or more of age, both parent and pediatrician tend to forget that the patterns of behavior forming during this time are the *anlage* of the complex processes of speech. Many of the speech defects which first command attention when the child is four or five have a history of development which extends back to birth or the first few months of life.

In this early period of growth, it is important for normal speech development that there be (1) normal physical and mental growth, (2) a "need for speech" in the sense that the child finds speech satisfying and rewarding in the social contacts and acceptance which it brings, and (3) an environmental stimulation in which language plays an important part. The prattling and the reassuring monologues with which so many mothers surround their babies have thus a practical development value beyond merely the social pleasure which it brings to mother and child.

The preschool and early school years bring peculiar environmental influences which also play a part in the origin and perpetuation of speech defects. The challenges of social life, too complex for the adjustment patterns of some children, lead to physical tensions and emotional disturbances which are quickly reflected in the speech and voice. Too much stimulation from the environment and the imposition of unrealistic educational and behavioral standards, when added to the normal strains of physical growth, prevent the child's speech from maturating normally. Sometimes mental and physical hygiene measures instituted in the period of development will bring about speech improvement without direct speech therapy. Even in those instances where speech therapy is needed for the preschool child, it is more likely to succeed if incorporated into a program of general care.

Physical Appraisal

A careful physical evaluation of the child is required to discover any existing or potential physical anomalies which can interfere with the development of normal speech. Essential for diagnosis, the examination also provides a basis for selective referral and treatment. A history of birth and development should be taken, and general observations of behavior should accompany the physical examination. In the examination particular attention should be paid to the following: (1) evidences of pre- or postnatal damage to the central nervous system; (2) disease, acute or chronic; (3) deficiencies in hearing and vision; (4) indications of abnormal physical growth; (5) nutritional status; (6) dental occlusion and oral hygiene; (7) evaluation of mental abilities, and (8) an estimate of personality and emotional health. Of these items, defects of vision and hearing, evidences of brain damage, and emotional immaturities are most often overlooked.

Three things which are frequently diagnosed as causative of speech defects deserve special mention in reference to the physical

examination: *tongue-tie*, *enlarged tonsils* and *adenoids*, and *mental retardation*.

Tongue-tie affecting speech is comparatively rare, and it is seldom that clipping the tongue aids in correction of an articulatory defect.

Tonsils and adenoids are sometimes removed in the hope that benefit to speech will result. If they are affecting the health of the child and if nasal breathing is hampered so that the child is a chronic mouth-breather, their existence will affect speech deleteriously. However, adenotonsillectomy performed simply on the off chance that it may help speech often brings no improvement, and sometimes real harm is done as in the case of the child with a cleft palate or a palate which functions poorly.

The mental abilities of a child with defective speech may be hard to assess; therefore, indications of mental deficiency in these children should be interpreted with caution. Although there is a high incidence of speech defects among children seriously retarded, there is not a correspondingly high incidence of mental deficiency among children with speech defects. In the organic (brain damaged) child, abnormal speech may be a function primarily of some specific brain damage rather than of any pervading intellectual deficiency.

Referral

When should the parents and the physician begin to feel concern about a child who shows abnormalities of speech development? Factors of age, general health, environment and trends of development must be considered for each child individually in answering this question. If the child is obviously making normal progress in motor development, in mental growth and in personality and social relationships, it is quite possible that an attitude of watchful waiting may be safely adopted, provided the speech defect is not so serious that it handicaps communication. On the other hand, the existence of a speech defect may in itself be symptomatic of maldevelopment and may point the need to a thorough appraisal of the child by the pediatrician in cooperation with the speech therapist.

The pediatrician may do much to assure normal physical development in these children, but he usually has neither the time nor the training to undertake speech therapy or direct counseling. Fortunately, he has a number of sources to which he can send children and their parents for guidance and training.

The public schools in the majority of our states now have some form of publicly supported speech correction service available to children of school age. In almost all of these states, the teachers who provide speech therapy are required to meet educational standards which guarantee clinical competency. A letter addressed to your State Department of Public Instruction should bring you information regarding the location of qualified speech therapists in the schools.

Most of our state supported universities and colleges and many of the large privately endowed schools maintain speech and hearing clinics which render direct diagnostic and treatment services in connection with professional training and research programs. Such clinics often work in close cooperation with the respective medical schools and, in some instances, are maintained as a part of the school. Medical referral to these clinics is usually welcomed, and the referring physician may obtain a detailed report of the findings and recommendations for therapy.

In addition to the service centers connected with educational institutions, there are therapists in private practice or in hospital clinics. In some cities, agencies such as the National Society for Crippled Children and Adults maintain service clinics in which speech correction is provided.

Information regarding qualified centers or professionally trained diagnosticians and therapists may be obtained from the American Speech and Hearing Association, Executive Secretary, Wayne University, Detroit, Michigan. Pamphlets suitable for distribution to parents of children are available through the National Society for Crippled Children, various State Departments of Public Instruction or through publications supplied by university clinics.

Raoul Dufy, Artist and Patient

FREDDY HOMBURGER*

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Shortly before he died, in his seventy-sixth year, Raoul Dufy arranged to bring to the medical profession of the United States some expression of his gratitude. He requested Merck & Co., Inc.—whose brand of cortisone was used in treating M. Dufy—to cooperate in this plan. The accompanying paintings, personally selected by M. Dufy are available without charge as 9" by 11" full color reproductions suitable for framing. Please write to Merck & Co., Inc., Department FS, Rahway, New Jersey.

THE Editors of POSTGRADUATE MEDICINE requested that I write a case history on Raoul Dufy's response to cortisone, and on March 20, 1953, I wrote him to ask his permission for the publication of his clinical record. On March 23 at 4:00 A.M. Raoul Dufy died suddenly, presumably of an intestinal hemorrhage.

FREDDY HOMBURGER

Portrait (by Raoul Dufy)

During our contact as physician and patient we had become close friends, and my feelings for him are such that this is not the time for much clinical discussion.

The world has lost one of its greatest artists and also one of the finest human beings; a man of an unequaled capacity to "see behind nature's tricks for beauty and to create beauty where none exists"; a human being with a wonderfully open mind and the trustful good heart of a child, yet the deep understanding and sympathy of one who himself has lived in joy and suffered to the full capacity of human senses. Dufy was egotist enough to live the life he knew was best for him as an artist, yet in doing so he was able to be more altruistic than most men in giving untold thousands joy through his creations. Medicine had the privilege of prolonging this creativity and thus to come to the aid of art.

At 73 years of age Dufy was our oldest patient receiving hormone therapy for rheumatoid arthritis. He was on continuous treatment from April 29, 1950, on doses ranging from 12.5 mg. per day to 200 mg. per day. Throughout his therapy it was necessary to balance the catabolic effects of cortisone by androgens and estrogens. Under this regimen a severe pre-existing osteoporosis actually improved during the three years of hormonal therapy. From the start we were concerned

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RAOUL DUFY

In the course of treatment with cortisone directed by Freddy Homburger in Boston, I stated that not only did the action of this remedy make itself felt on my rheumatism, but as well on my general mental activity. It is a phenomenon that reminded me of the one I had experienced during a vacation in Sicily where, under the action of the light of Syracuse, it appeared to me that I understood everything much better, in a word, that I had become more intelligent. The same adventure with cortisone made me say to Homburger that his treatment was equally good for painting.

Raoul Dufy

Forcalquier, France
14th November 1952

about the state of the arteries in this patient. But aside from a gluteal abscess early in the course of treatment before all hormones began to be taken by mouth, occasional edema when dietary rules were ignored and the development of obesity, his course was free from complications.

When I first saw the patient he was unable to move from his wheel chair or bed without much assistance, and every motion was painful. He could not lift his food to his mouth, and while he was still able to paint, this was agony in spite of much aspirin and codeine. During the last three years of his life while on hormone therapy, he painted with ease, could move about without much help, and had no difficulties using his hands for eating, drinking and dressing. He told me cheerfully in May 1952 in Paris that he was having a wonderful time, that he did not wish to adhere too closely to any dietary restrictions because he felt that one should not spend one's last years being careful and not enjoying one's self. When told by more cautious people he was a fool, he replied that "cautious people who pass judgment on fools see no further than their noses. Only a fool knows the consequences of his acts!"

As his French physician, Dr. Rene Fauvert of Paris, wrote me after Dufy died: "Finally our friend has died as he would have wished to go, upon his return from an excursion through the countryside, without having had to interrupt his work. He painted until his last day and it is indeed to you that he owed this."

From what we hear through his French physicians, Dufy did not die as a consequence of his treatment. However, the dangers of continued cortisone treatment at his age were often discussed with him freely and fully. He accepted these risks and we feel that all too much caution prevails among physicians in many cases of rheumatoid arthritis of the aged when it comes to balancing the advantages of cortisone against its side effects and toxicity.

This man was a happy man during most of his last years, whereas he might well have been desperate without the aid of cortisone. And we, who remain, are richer because the sun and the brilliance, the joy and lightheartedness had returned to many a Dufy canvas and water color in the productive period preceding his death. In 1952, he wrote to me that could he live to 85 he was certain he could round out his work. He was his own severest critic and asked for too much time. Today, his artistic achievement stands complete and unique before his grateful friends and admirers.

His personal friends will always sadly miss Raoul; for his wide art-loving public Dufy has never departed and lives forever. Thanks to cortisone, he had three added years of productivity and enjoyment, and we possess some 200 more of his works than there would have been without it.

The Artist's Studio

Raoul Dufy

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Raoul Dufy

The Regatta at Henley

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Raoul Dufy

Two Bridges Over East River

Raoul Dufy

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The Beach Raoul Dufy

Homage to Claude Debussy Raoul Dufy

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THE RISE AND FALL OF CALOMEL

ONLY a generation ago mercurous chloride was a widely used drug; today it is almost discarded and forgotten. Few, if any other, medicines have been credited with such a diversity of actions—cathartic, diuretic, antiluetic, antiseptic, antiphlogistic, antipruritic, sedative and alterative. Does such a drug deserve to fall into oblivion? A review of the history of this panacea will probably not answer this question, but it does shed interesting light on the progress of therapeutics.

Calomel occurs in nature as a mineral named "horn quicksilver," but the process for making it was first described in the seventeenth century in the Basilica Chymica of Oswald Crollius. It was named "arcanum Corallinum seu mercurius sublimatus noncorrosivous," but soon received other names, including draco mitigatus, laudanum minerale and mercurius dulcis. In the early seventeenth century de Mayerne, the physician to Henry IV of France, is said to have coined the name calomel. La Wall,* from whose delightful book this paragraph is abstracted, states that the etymology of the word is in doubt; others derive it from the Greek *kalos*, meaning beautiful, and *melas*, black, because calomel is white although formed from black materials. Much later the last syllable was thought to have come from the Greek *mele*, meaning honey, and so calomel was sometimes called sweet mercury.

For many years calomel was one of the mercurials used in the therapy of syphilis, but it fell into disfavor because of its marked action on the digestive tract. To avoid this, it was tried by fumigation without success. Calomel, however, continued to be employed as a purgative; and in the years around 1800, it was in America the drug of choice for colic. Certainly many cases of so-called colic were actually acute appendicitis, and the resulting purgation and perforation often must have led to peritonitis. But as we will see calomel was to become the drug of choice in the treatment of peritonitis.

The belief in calomel as a remedy for inflammations and infections dates back at least to the end of the eighteenth century, at which time Graves, of thyroid fame, was in Dublin giving large doses for inflammations. A few years earlier Benjamin Rush considered it the "sovereign" remedy in yellow fever, typhus and other malignant affections. He gave it routinely, along with jalap and repeated bleedings, to all patients in the epidemics of yellow fever in the latter part of the eighteenth century in Philadelphia. But whether he credited it with antiphlogistic power is hard to tell. Rush always treated vigorously, giving calomel in 10 gr. and jalap in 15 gr. doses, repeated frequently. His claims for unusual success with yellow fever are hard to accept, but equally difficult to deny.

*La Wall, Charles H.: Four Thousand Years of Pharmacy. Philadelphia, Lippincott Co., 1927.

During the nineteenth century, calomel was the subject of much argument. Was it a cholagogue acting to increase the discharge of bile? Certainly the stools turned green, but was this due to an increase of bile or to the presence of some form of mercury itself; or was it the result of the antiseptic action of calomel preventing the decomposition of biliverdin? Another question concerned the possibility of calomel being converted by the "gastric juices" into corrosive sublimate; this was the old name for mercuric chloride.

Finally the problem of dosage worried the wise men of that day. It had long been observed that there was little difference in the purgative effect of small or large doses. A few doses of ⅛ gr. are as efficient as 10 gr., a dose incidentally which was often given to infants. An ounce was occasionally administered to an adult, and there is one report that a patient with cholera received a pound "without visible effect." The explanation is probably to be found in the relatively small amount of mercury absorbed from the gastrointestinal tract when calomel is ingested. Incidentally it was believed that large doses acted as a sedative, which explains the name laudanum minerale of 200 years before.

None of these questions was then answered satisfactorily, but calomel continued to be prescribed as a cholagogue, cathartic, antiluetic and as a specific for inflammation and infection, especially of the digestive tract. In 1885 a leading American text recommended it for hookworm infestation, cholera morbus and infantum, enterocolitis, acute gastritis, acute intestinal catarrh, catarrh of the bile ducts, and in jaundice for the vomiting and diarrhea.

In 1906, less than 50 years ago, H. C. Wood, in the thirteenth edition of his authoritative text on Therapeutics, still accepted the virtues of calomel as the following abstracts will testify:

"Calomel should not be used in *adynamic inflammation* or where exudation is serous rather than fibrinous. In *puerperal peritonitis* it has been strongly advocated by some and as strongly condemned by others, simply because there are two varieties of the disease, the *sporadic* or *sthenic*, and the *epidemic* or *asthenic*; and in the one both bleeding and calomel are strongly indicated, while in the other they are effective only for evil."

In catarrhal jaundice he believed calomel, as a cholagogue, did good "but even to a greater extent by its antiphlogistic power . . ." It should be administered "until the gums are rendered slightly sore." Both the word antiphlogistic and the deliberate production of even mild mercurial ptyalism are today in the limbo of forgotten things.

Wood advised calomel as a cathartic and also as a diuretic, without any worry about it causing harmful damage to the kidneys. In biliousness it was especially indicated, and was of value if the stools were clay colored unless an organic lesion was present.

Calomel was not the only drug in common use at the turn of the century about whose action there was much argument. It was one of a group of medicaments classified as Alteratives, about which group Wood wrote: "There are employed by practitioners of medicine, to affect certain diseases most intimately connected with the processes of nutrition, various substances which do not, at least in doses commonly used, produce any very obvious symptoms. It is to medicines of this character that the name of *Alteratives* has been applied, because when administered they seem simply to alter morbid processes." In this group were phosphorus, zinc, arsenic, calomel, gold, iodine, cod liver oil, colchicum, thyroid body, suprarenal capsules, pituitary body, spleen, thymus and many others.

It is certainly amazing to read this list, which had to be learned in medical school by the writer of this editorial, and to consider the advances of the past 45 years. A student of those days has surely had to alter his opinion about the Alteratives—some of which have been found to have a great potency and value. He has had to learn much about those now named hormones and vitamins, and to discard others. Gold alone, perhaps, continues to be employed with little sure evidence of its value, and quite in the fashion of the old Alteratives.

Calomel is not quite forgotten. In recent

texts it is mentioned as a cathartic, a diuretic and for the relief of the itching of cirrhosis of the liver! Also it is used in powdered form for application to corneal lesions. Do these latter two uses hark back to the days when calomel was a cholagogue and an antiphlogistic? The current literature contains perhaps a dozen articles chiefly concerned with its toxic and allergic effects.

Possibly calomel deserves this fate, but it is permissible to ask whether its almost 300 years of popularity and its many supposed virtues do not suggest that its present oblivion may not be the result in part of excessive dosage, in part of unjustified claims, and also of the invasion by well advertised and more profitable substitutes? Something very useful has come from the "suprarenal capsules"; perhaps our old friend, calomel, should be given another chance to prove whether or not it deserves a place in modern therapy.

O. H. PERRY PEPPER

IMMUNIZATION AGAINST POLIOMYELITIS

EARLY in 1953 Dr. Jonas E. Salk of the Virus Research Laboratory in the University of Pittsburgh School of Medicine reported that antibodies against poliomyelitis could be stimulated by inoculating intramuscularly a vaccine prepared with tissue culture fluid treated with formalin, emulsified with mineral oil. The studies have been extended and the results were presented by Dr. Salk before the meeting of the American Academy of Pediatrics in Miami, Florida, in October. Now he has announced that it is possible to stimulate formation of antibody to the three types of poliomyelitis virus in human subjects without, as well as with, the mineral oil adjuvant. When antibody was present before vaccination, a further rise occurred, indicating that the inoculation has a booster effect. Children and adults who do not have antibody to any of the poliomyelitis viruses can form antibody to the three virus types.

Another observation reported by Dr. Salk is the extraordinary height to which antibody level can be raised in persons who have some antibody initially. Moreover, he is able to state unequivocally that the results are due to the antigenic substance in the inoculum and to any particles of living virus that may be *postulated* to be present. Antibody induced by injections of aqueous vaccines has been shown to persist for periods of three to four months. Indeed, persistence may be longer, but conclusions cannot yet be drawn concerning the total persistence of antibody until sufficient time has elapsed and a sufficient number of serums have been tested.

In the second group of persons studied, comprising 474 in all, most were children, but there were 53 persons 18 years of age or over, and less than half of them had initial antibody for all three types of virus. In none of those included was there any evidence of illness attributable to the inoculations. The longest interval for the initial group inoculated has been one year. A number of samples drawn at seven months from the first group showed no decline in the titer.

The positive results reported have led logically to the next step which is a large scale inoculation of hundreds of thousands of children to be undertaken next spring. This will probably be a controlled study involving the injection of alternate children with either vaccine or a control preparation consisting of either another biologic preparation, such as a vaccine for another disease, or of physiologic salt solution.

Tentatively an experiment has been proposed involving the inoculation of some 600,000 children distributed over 100 counties, with a similar number of controls. For such an experiment the preparation is difficult and arduous. Already growth of tissue cultures is under way in one great commercial laboratory and another agency is preparing to manufacture the vaccine. The purpose of the study is to determine to what extent the incidence of naturally occurring infantile paralysis can be influenced by such inoculations. Competent scientists and statisticians are preparing to administer the experiment and to record the results.

The point now reached in progress toward the complete elimination of crippling infantile paralysis is an awe-inspiring peak in medical achievement. This accomplishment was not an accident. Step by step, with the inspiration and magnificent support of the National Foundation for Infantile Paralysis, investigators have fought forward for 15 years. The steps have included isolation and then typing of the viruses, cultivation of viruses on tissue, immunologic studies of the effects of various forms of vaccine on the ability of the body to develop resistance, and, now in prospect, a crucial experiment on a scale never previously attempted in such investigations. The support of this work has involved the expenditure of many millions of dollars of funds voluntarily contributed by the people of the United States who, year after year, have shown their confidence that success would ultimately be achieved in the battle against this most feared of all the conditions that affect children. How glorious and how inspiring it is to contemplate the victory that is now in sight!

MORRIS FISHBEIN

BLOOD PRESSURES OF PERSONS OVER 65 YEARS OLD

THE name of Dr. Arthur M. Master is known to thousands of physicians all over the world for his development of new standards for evaluating measurements of blood pressure in human beings. Estimation of blood pressure is among the most frequent of all medical procedures, and the correct interpretation of readings is of utmost importance. The incidence of hypertension increases with age. Usually an arbitrary figure, 150/90, has been considered the upper limit of normal for adults over 40 years old. Extensive recordings were made of the blood pressures of over 74,000 workers up to the age of 64 and the upper limit was found to be higher for each age group than the figures previously used.

With continuous increase in life expectancy many more people now reach advanced years than did so formerly. Many millions of people in our population—perhaps in excess of 12 million—are now over 65 years old. Now Dr. Arthur M. Master and Dr. Harry L. Jaffe, representing the New York Heart Association and Mount Sinai Hospital of New York, and Herbert H. Marks for the Metropolitan Life Insurance Company have undertaken a new study to find out the normal range of blood pressure for persons over 65, whether or not the blood pressure continues to increase with age and to vary with sex in persons over 65, and the relationship of blood pressure to weight, to surface area and to height. Recent studies have failed to reveal any important relationship between hypertension and coronary occlusion in men, although such a causal relationship does exist in women.

In undertaking these new studies the investigators have been stymied by the difficulty of access to the persons to be studied. Industry is not a suitable source because relatively few persons 65 or over are employed. One-half the industries routinely discharged workers whose blood pressures were beyond certain arbitrary limits, varying incidentally from 140/90 to 230/130. In old age homes only scanty data are available regarding blood pressures. Therefore, questionnaires were sent recently to 17,000 physicians asking them to examine six persons in their practices, two each in the age groups 65 to 69, 70 to 74 and two above 75 years of age. All were to be in fairly good health, although chronic disease was not to be a cause for elimination. Special cards for recording examinations were supplied. The number of responses, representing a fraction of a per cent, has been disappointingly small.

Here is an opportunity for physicians to participate in a significant piece of research which will yield results important both for them and their patients.

MORRIS FISHBEIN

Physicians interested in further information on this study may write to: Blood Pressure Study, 11 East 100th Street, New York 29, New York.

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► MODERN CONCEPTS IN MEDICINE

By Julius Jensen, Ph.D. (in Medicine), University of Minnesota, Minneapolis. 636 pages, illustrated. 1953, The C. V. Mosby Company, St. Louis. $11.50.

The author has attempted to integrate physiologic and biochemical principles with the disease entities of internal medicine. This is in accord with the current concept that a proper understanding of disease is based not only on recognition of the clinical manifestations of disease but also on knowledge of the basic mechanisms that give rise to disease.

The text is divided into 4 parts containing a total of 25 chapters. Part 1 is an introduction consisting of a history of the development of current concepts in medicine, and a brief review of cellular structure and activity and the principles of adaptation. Part 2 deals with cellular metabolism, fluid and electrolyte balance, hydrogen-ion concentration, regulation of temperature of the body, immune reactions and neoplasm. Part 3, which makes up most of the text, is concerned with infectious diseases and diseases of the various organ systems of the body. Part 4 is mainly devoted to enzymes, vitamins and the nervous system.

Although the book is interesting, it is not recommended because of sketchy and inadequate coverage of its subject matter. In attempting to incorporate into a short text pertinent information from the vast fields of physiology, biochemistry and internal medicine, the author has omitted many fundamental and essential facts, thereby detracting from the value of his book. In general, the material presented in this book is readily obtainable and more adequately discussed in the current, standard textbooks of internal medicine and medical biochemistry and physiology.

R. V. R.

► AMEBIASIS; Pathology, Diagnosis and Chemotherapy

By Hamilton H. Anderson, M.D., Professor and Chairman, Pharmacology and Experimental Therapeutics; Warren L. Bostick, M.D., Associate Professor of Pathology, Department of Pathology, and Herbert G. Johnstone, Ph.D., Professor of Parasitology, Parasitology and Mycology Section of the Department of Medicine, School of Medicine, University of California Medical Center, San Francisco. 431 pages with 119 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $11.50.

This monograph by the University of California group represents a very comprehensive survey of the trials and tribulations encountered in studying the endemiology, etiology, pathogenesis, pathology, symptomatology, laboratory diagnosis and chemotherapy of amebiasis. In the 40 years since Colonel Vedder demonstrated the effectiveness of emetine *in vitro* as an amebicide, a variety of therapeutic procedures have been developed throughout the world.

Chauncey Leake and associates in this California group performed studies leading to the development of carbarsone and VIOFORM®. Subsequent investigations have confirmed the value of these agents and indicated the possibility of additional therapeutic agents such as DIODOQUIN® and chloroquine, with suggestions that TERRAMYCIN® and fumagillin may have safer activity than emetine in this field. Various strains of *Endamoeba* are discussed although special interest is directed to *E. histolytica*. For the latter an entire chapter is dedicated to discussion of requirements for growth and cultivation in culture media.

Each of the 13 chapters is complete in itself and carries its own bibliography. An author and a subject index appear very adequate, comprising 58 pages.

(Continued on page A-81)

The summary of the entire book recommends closer integration of laboratory studies on the essential metabolism of *E. histolytica* and clinical investigations as the basis for more rational chemotherapy.

J. C. M.

► THORACIC SURGERY AND RELATED PATHOLOGY

By Gustaf E. Lindskog, M.D., William H. Carmalt Professor of Surgery, and Averill A. Liebow, M.D., Professor of Pathology, Yale University School of Medicine, New Haven, Connecticut. 644 pages with 285 figures. 1953, Appleton-Century-Crofts, Inc., New York. $15.00.

Textbooks, as a rule, lag far behind current thinking. This might be expected to be particularly so in a rapidly expanding field such as thoracic surgery. Drs. Lindskog and Liebow have, however, overcome this difficulty to a remarkable degree in their new book. This is certainly the most complete and up-to-date book on thoracic surgical disease now available. While other contemporary books on this subject have stressed details of operative technic, the authors have chosen to consider the broader aspects of thoracic surgical disease, including anatomy, physiology and pathology.

The book is well and amply illustrated with photographs of pathologic specimens and roentgenograms from the extensive clinical material of the Grace-New Haven Community Hospital, New Haven, Connecticut. This is not an exhaustive work, weighed down by minutiae, but a clearly written and concise discussion of the pertinent facts. Those interested in the finer points of controversial subjects must seek their information elsewhere. Included are thorough considerations of the diagnosis and treatment of such subjects as trauma, infections, congenital abnormalities, benign and malignant neoplasms and functional disorders that may affect the thorax and its contents. Each chapter is well documented with an ample bibliography.

Long sections have been devoted to pulmonary tuberculosis and cardiovascular surgery. The authors have wisely elected to include discussions of various collapse procedures in the treatment of pulmonary tuberculosis, in spite of current enthusiasm for resectional surgery. The

(Continued on page A-82)

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section of cardiovascular surgery would have been more complete, however, had a separate chapter been devoted to cardiac catheterization.

One of the outstanding features of the book is the excellent pathologic discussion on each of the subjects represented. Dr. Liebow's wide experience in the pathology of thoracic disease and in the investigative aspects of pulmonary and bronchial vascular changes in pathologic conditions of the lungs has amply prepared him for the task.

F. H. E.

► PERSONALITY MANIFESTATIONS IN PSYCHOSOMATIC ILLNESS; Visual Aid Charts to Psychotherapy

By O. Spurgeon English, M.D., Chairman, Department of Psychiatry, Temple University Medical School, Philadelphia. 57 pages. 1953, Edward Stern and Company, Inc., Philadelphia.

In this thin, inexpensive, easily handled volume, the chairman of the Department of Psychiatry at Temple University Medical School presents highly graphic, dramatic, visual pictures of nine frequently seen psychosomatic disorders accompanied by verbal summaries of the conditions and their treatment. The charts were developed out of a need to portray visually the interplay between emotions and various end organs; it is specifically stated that they are intended as part of the process of psychotherapeutic orientation, not as a treatment substitute.

The charts are intended for patient use, albeit under the supervision of a physician; the written material tends to be disproportionately technical, however, and one suspects that few physicians, much less patients, will have any useful understanding of "unconscious hostility" or "limited renunciation capacity." The charts are startling in their tendency to caricature the suffering of patients, a trend which may seem to emphasize the physician's awareness of discomfort, but one which hardly seems to justify the dramatization which is present. The charts show in a general and repetitive fashion the interplay of feelings and organ systems but contain no specific, workable information about such interchange. The initial chart depicting this autonomic nervous system is useful but oversimplified for the medically sophisticated patient.

The written material would seem to be of benefit to the busy practitioner as a preview of the common psychosomatic disorders. The summaries of obesity and dysmenorrhea are particularly clear in their emphasis on the importance of emotional factors and the futility of chasing hormonal shadows. Handicapped by the goal of brevity, Dr. English has implied that the possibility of quick cures by means of intellectual understanding. Such does not occur in the handling of psychosomatic disorders. The creating of such a distortion can only frustrate the physician and jeopardize the patient's health. There is undoubtedly a use for the present volume, but primarily as a part of the very earliest, initial orientation of the emotionally disturbed patient toward psychiatric attitudes rather than as a tool in true therapy.

M. G.

► ENDOCRINOLOGY IN CLINICAL PRACTICE

Edited by Gilbert S. Gordan, M.D., Assistant Professor of Medicine, University of California School of Medicine and H. Lisser, M.D., Clinical Professor of Medicine and Endocrinology, University of California School of Medicine, San Francisco. 407 pages, illustrated. 1953, The Year Book Publishers, Inc., Chicago. $10.50.

The objective of this book is to provide the practicing physician with the knowledge necessary for the diagnosis and treatment of most endocrine disorders. The practical approach is stressed, while theoretical aspects and controversial points are not discussed at length.

Thirty members of the clinical and full time staff of the University of California School of Medicine have contributed to the book, each writing about those aspects of glandular disease with which he has had extensive clinical experience.

The introductory chapter deals with specific points in taking a proper "endocrine" history, the physical examination, laboratory aids in diagnosing endocrine disease, and the underlying principles of endocrine therapy. Successive chapters are devoted to the thyroid, parathyroid and metabolic bone disease, the pituitary, adrenals, carbohydrate metabolism, obesity and leanness, the gonads, infertility, and endocrine therapy of neoplastic diseases.

An appendix presents most useful and practical guides for the application of endocrine

(Continued on page A-84)

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as present in concentrated extractives from streptomyces fermentation	
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preparations with stress given to the details of administration and an explanation of the characteristics of the proprietary drugs and compounds. Excellent photographs illustrating the various endocrinopathies are included.

T. B. C.

► MANIC-DEPRESSIVE DISEASE: Clinical and Psychiatric Significance

By John D. Campbell, M.D. 403 pages. 1953, J. B. Lippincott Company, Philadelphia, London and Montreal. $6.75.

The general physician as well as the psychiatrist will find this a book on modern treatment of one of the most common neuropsychiatric disabilities—cyclothymia or manic-depressive disease. This is not a theoretical treatise, but a useful, down-to-earth manual for the diagnosis and treatment of the depressed, nervous men, women and children who come to the general practitioner, pediatrician and internist. Dr. Campbell shows how the disease may be recognized early in its course.

Instead of delving into the unconscious, the author shows that many patients are suffering from endogenous cycles of mood disturbances, and he states in detail what can be done to prevent these cyclothymic disorders. The author takes a new approach to manic-depressive disease; he presents it as a physiologic disturbance in the autonomic nervous system. An entirely new group of symptoms is presented as they were observed in a large number of manic-depressive patients. These have not heretofore been recognized as symptomatic of the disease. Dr. Campbell writes of a two to six year study in which his cases consistently showed autonomic disturbances. The general physician and internist will recognize these illustrative cases as similar to those in his own daily practice.

The latest research in the diagnosis and treatment of manic-depressive disease is also discussed. The association between the hypothalamus, pituitary and adrenal glands is taken up in detail. The importance of ACTH, the role of stress and fatigue and the latest research on how electroshock therapy functions are reviewed.

Sections are devoted to the social complications of the disease—alcoholism, religion, marital problems, divorce, suicide. Included is a section on manic-depressive psychosis in children, a seldom described occurrence. This new, informative work of scholarly quality should become a notable contribution to the literature on psychosomatic medicine and psychiatry.

R. H. K.

► THE PRACTICAL MANAGEMENT OF PAIN IN LABOUR

By W. D. Wylie, M.A., Anaesthetist to St. Thomas's Hospital and The National Hospital for Nervous Diseases, London, England. 148 pages, illustrated. 1953, The Year Book Publishers, Inc., Chicago. $3.50.

The author of this monograph—a medical anesthesiologist from London, England—has attempted to enunciate principles and practices which are of value for the relief of pain in labor. In the preface he stresses the need for cooperation between the anesthetist and the obstetrician. In the absence of such specialized services, the physician in charge must have a practical knowledge of analgesia and anesthesia as applied to parturition.

Introductory chapters deal with anatomic and physiologic considerations, analgesic and anesthetic agents and apparatus used for administration of volatile drugs. These chapters are well illustrated with diagrams and photographs.

The remaining chapters deal with methods of pain relief in normal and abnormal labor. Separate chapters are devoted to cesarean section, local analgesia, and the use of anesthetic and analgesic agents for the therapy of venous thrombosis, toxemia of pregnancy, and anuria.

As do many British writers, the author has a literary style which makes for easy reading. The facts are presented in a concise and orderly manner. The principles stated are sound and conform to the best practices in this country as well as in Britain. Although the terminology differs for the drugs used, a page of American equivalents is given to clarify the nomenclature. The use of paracervical block and Abrams conduction analgesia are not mentioned, but this is not surprising in view of the limited use of these procedures in current practice.

Because of its wealth of accurate information based on sound conservative principles, this small text should prove valuable for any physician called on to administer drugs for the relief of pain in labor.

M. B. S.

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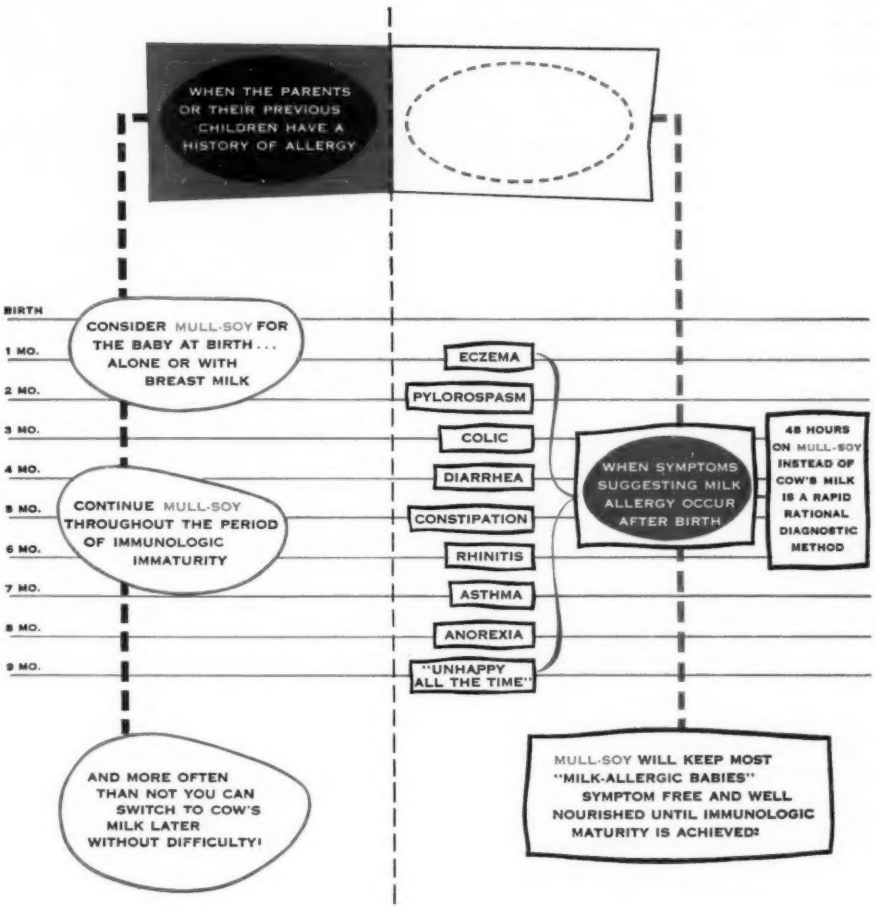
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1. Glaser, J., and Johnstone, D. E.: Ann. Allergy 10:433, 1952.
2. Clein, N. W.: Ann. Allergy 9:195, 1951.

Books received will be acknowledged in this department each month. As space permits, books that are of principal interest to our readers will be reviewed more extensively.

The Action of Insulin. By Niels Haugaard, Ph.D., Assistant Professor of Physiological Chemistry in Research Medicine, School of Medicine; and Julian B. Marsh, M.D., Assistant Professor of Physiological Chemistry, Graduate School of Medicine, University of Pennsylvania, Philadelphia. 113 pages. 1953, Charles C Thomas, Springfield, Illinois. $3.75.

Modern Clinical Psychiatry. By Arthur P. Noyes, M.D., Superintendent, Norristown State Hospital, Norristown, Pennsylvania. Ed. 4. 609 pages. 1953, W. B. Saunders Company, Philadelphia & London. $7.00.

A Primer of Cardiology. By George E. Burch, M.D., Henderson Professor of Medicine, Tulane University School of Medicine, New Orleans. Ed. 2. 339 pages with 214 illustrations. 1953, Lea & Febiger, Philadelphia. $5.50.

Lecture Notes on the Use of the Microscope. By R. Barer, M.C., University Demonstrator in Anatomy, University of Oxford, Oxford, England. 76 pages with 8 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $2.00.

Atlas of Regional Dermatology. By Ernest K. Stratton, M.D., Research Associate, The George Williams Hooper Foundation for Medical Research, University of California Medical Center, San Francisco, California, and contributing authors. 288 pages, 596 illustrations (25 in color). 1953, Charles C Thomas, Springfield, Illinois. $15.00.

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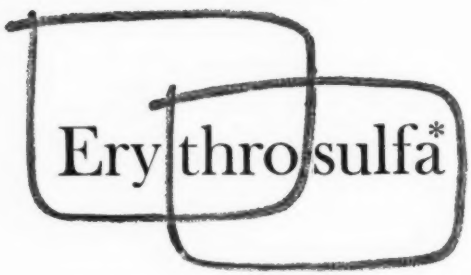

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The Heart Beat: Graphic Methods in the Study of the Cardiac Patient. By Aldo A. Luisada, M.D., Associate Professor of Medicine and Director, Division of Cardiology, The Chicago Medical School, Chicago, Illinois. 527 pages with 311 illustrations. 1953, Paul B. Hoeber, Inc., New York. $12.00.

Clinical Tropical Diseases. By A. R. D. Adams and B. G. Maegraith, School of Tropical Medicine, Liverpool, England. 508 pages with 65 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $10.50.

Living with a Disability. By Howard A. Rusk, M.D. and Eugene J. Taylor, in collaboration with Muriel Zimmerman, O.T.R. and Julia Judson, M.S. 207 pages, illustrated. 1953, The Blakiston Company, Inc., Garden City, New York. $3.50.

Sexual Behavior in the Human Female. By Alfred C. Kinsey, Wardell B. Pomeroy, Clyde E. Martin, Paul H. Gebhard, Research Associates; and others on the staff of The Institute for Sex Research, Indiana University. Foreword by Robert M. Yerkes and George W. Corner. 842 pages with 151 charts, 179 tables and 4 illustrations. 1953, W. B. Saunders Company, Philadelphia and London. $8.00.

The Year Book of Medicine. Edited by Paul B. Beeson, M.D., Carl Muschenheim, M.D., William B. Castle, M.D., Tinsley R. Harrison, M.D., George B. Eusterman, M.D. and Robert H. Williams, M.D., 736 pages, illustrated. 1953, The Year Book Publishers, Inc., Chicago. $6.00.

Inhalation Therapy and Resuscitation. By Meyer Saklad, M.D., Director, Department of Anesthesiology, Rhode Island Hospital, Providence. 343 pages with 130 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $7.50.

Report of 8th International Congress of Rheumatic Diseases. 1 volume, 292 pages. 1953, Médecine et Hygiène, 15 Boul. des Philosophes, Geneva, Switzerland. 25 Swiss francs.

Clinical Disorders of the Heart Beat. By Samuel Bellett, M.D., Director, Division of Cardiology, Philadelphia General Hospital, Philadelphia, Pennsylvania. 373 pages, with 164 illustrations. 1953, Lea & Febiger, Philadelphia. $8.50.

Manual of Medical Emergencies. By Stuart C. Cullen, M.D., Professor of Surgery; Chairman, Division of Anesthesiology, State University of Iowa College of Medicine, and E. G. Gross, M.D., Professor and Head of Department of Pharmacology, State University of Iowa College of Medicine, Iowa City. Ed. 2, 278 pages with 34 illustrations. 1953, The Year Book Publishers, Inc., Chicago. $4.50.

Managing Your Coronary. By William A. Brams, M.D., Senior Attending Physician, Michael Reese Hospital, Chicago. 158 pages, illustrated. 1953, J. B. Lippincott Company, Philadelphia & New York. $2.95.

The People's Health; A History of Public Health in Minnesota to 1948. By Philip D. Jordan, Ph.D., Professor of History, University of Minnesota, Minneapolis. 524 pages, illustrated. 1953, Minnesota Historical Society, St. Paul. $5.00.

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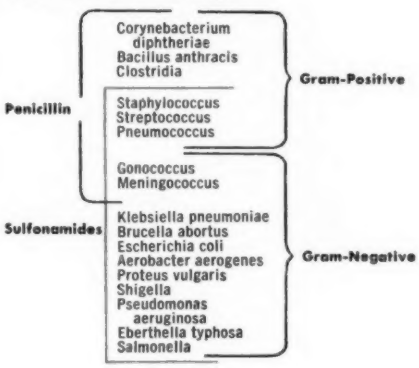

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